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VOLUME 246 MAY 1, 1952 NUMBER 18

"Hysteria" in Men 677
Eli Robins, James J. Purtell and Mandel E. Cohen

Conduction of Visceral Pain 686
James C. White

Chronic Ulcerative Colitis and Pregnancy . . 691
Marcel Patterson and Ernest J. Eytinge

Rupture of the Uterus During Pitocin Infusion 694
James Henry Ferguson, George T. Schneider and Henry K. Miller

Medical Progress: The Significance of Cholesterol in the Pathogenesis of Vascular Lesions 695
S. J. Thannhauser

Medical Intelligence: Acute Intestinal Obstruction Caused by Macaroni 702
David Pecora, Enrico Pepe and Philip Cooper

Case Records of the Massachusetts General Hospital 704

Editorials:
The Annual Meeting 711
Epidemic Hemorrhagic Fever 712
Health and Wealth in Old New York 714
Token of Authority 714

Massachusetts Medical Society. 714, 716

Notices 715, 720

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Volume 246 MAY 1, 1952 Number 18

"HYSTERIA" IN MEN

A Study of 38 Patients So Diagnosed and 194 Control Subjects

ELI ROBINS, M.D.,† JAMES J. PURTELL, M.D.,‡ AND MANDEL E. COHEN, M.D.§

BOSTON

PRIOR to 1618, hysteria was said to occur only in women. The writings of Hippocrates,[1] Galen,[2] Aretaeus[3] and Celsus[4] make clear their belief that the condition never occurred in men. Caroli Pisonis (Charles Lepois),[5] in 1618, was probably the first to suggest that hysteria could occur in men as well as in women. Since then, many authors[6-19] have reported what they term hysteria as occurring in men, although the frequency is low in men as compared with that in women.[6, 7, 9, 10] Briquet[6] found that in 430 cases diagnosed hysteria only 1.6 per cent occurred in men; Savill,[9] from a study of 500 cases, reported "over 97 per cent of hysterics are females"; Charcot[7] estimated that less than 5 per cent of cases occurred in men; and Weir Mitchell[10] agreed that the condition was rare in men. In a study made in this laboratory,[20] 91 cases of hysteria, all in women, were observed in a civilian hospital at which the proportions of male and female admissions were about equal. No cases were found in men.

The work described in this report was undertaken to study hysteria in men and to test a clinical impression that the illness in men presented different manifestations from those noted in women. The objectives of this study were two — to describe by the use of a quantitative and controlled method the clinical nature of the disorder as it is diagnosed in men, and to learn whether the condition as found in men differs from that found in women.[20]

PROCEDURE

Searching for, Locating and Determining the Criteria for Selecting the Male Study Group

A search was made for men with hysteria in a civilian diagnostic hospital and on the medical and neurologic services of a large municipal hospital. Criteria for the diagnosis included special symptoms, course, manner and attitude during examination.[20] During the period of this search 2274 patients were admitted to the diagnostic hospital. Three hundred and eighty-eight consecutive referrals to the psychiatric service were examined by one or more of the authors. Of these 388 patients, 121 of them were men. In addition, house officers and the psychiatric consultant of a large municipal hospital were asked to watch for such cases and to refer them for special examination for this study. This source of patients was considered supplementary to the consecutive examination of the diagnostic hospital patients. No case of hysteria in a man was found in either hospital.

Since no men with typical hysteria were discovered in civilian hospitals, and since the term is an acceptable diagnosis in service and Veterans Administration hospitals, cases¶ were searched for and examined in these facilities. In all, 38 men were found, including 20 soldiers, 1 coastguardsman, 13 veterans and 4 civilian patients with monetary compensation problems. The 20 soldiers represented 3 per cent of a total of 672 patients examined by one of the authors in an Army hospital during an eleven-month peacetime period when there were no combat problems to be considered. Of 13 veterans, 2 were examined at a civilian diagnostic hospital, 4 at a Veterans Administration hospital, 1 at a Marine hospital and 6 in a Veterans Administration mental-hygiene clinic. To obtain an approximation of the frequency of the diagnosis hysteria ("conversion reaction") as made by Veterans Administration psychiatrists, 1194 consecutive records from the Veterans Administration mental-hygiene clinic were reviewed. Sixty-three of these patients (5.3 per cent of the total) had a recorded diagnosis of "conversion reaction." Two civilian patients were examined at a Marine hospital and 2 others at a civilian diagnostic hospital. These 4 patients had been hospitalized for "compensation" problems.

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This study was supported by a research grant from the Medical Department, U. S. Army, and carried out with the co-operation of the Veterans Administration.

Patients and control subjects were studied in the psychiatric and medical services of the Joseph H. Pratt Diagnostic Hospital, the Murphy General Hospital (Army), Brighton Marine Hospital (United States Public Health Service), the Massachusetts General Hospital Cardiac Research Laboratories, Boston City Hospital (Harvard Medical and Neurological Services), Veterans Administration Hospitals (Cushing, Bedford), the Veterans Administration Mental Hygiene Clinic, Boston, The Malden and Melrose Gas Light Company and the General Electric Company, Lynn, Massachusetts.

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¶Hysteria patients are classified under various terms in VA and army hospitals; only those termed "conversion reaction" were included in this study.

The following criteria were used: (1) Other physicians had diagnosed the illness as hysteria or "conversion reaction" or had concluded that the patient belonged in the "neurosis" group. (2) No other diagnosis was established by anyone to explain the symptoms and the authors agreed that the clinical picture was not explained by any other medical, surgical or neuropsychiatric diagnosis. (3) The patient had among his symptoms at least one of the following: amnesia, fits, unexplained pain, vomiting, urinary retention, blindness, paralysis, trances, impotence or aphonia. These particular symptoms were chosen because they represented the authors' estimate of present-day ideas concerning the characteristic symptoms of hysteria.* This estimate was made on the basis of common usage, such as terminology in textbooks[16-19] and general clinical practice.

Selection of the Control Groups

Healthy men. Thirty-nine healthy men were control subjects. Twenty-four were soldiers whom commanding officers regarded as healthy, "good" or "excellent" soldiers with no chronic illness, and 15 were healthy civilian employees of a utilities company. These employees had good to excellent work records. None of the soldiers refused examination; of the 16 civilians, 1 refused. The mean age was 35.9 years; the range was nineteen to sixty years.

Men with chronic medical illnesses. Thirty-one men with chronic medical illnesses, which included, among others, duodenal ulcer, bronchial asthma, chronic glomerulonephritis, gastric carcinoma and Hodgkin's disease, were examined as controls. Twenty-two of these were hospitalized soldiers and 9 were hospitalized civilians; none refused examination. The mean age was 35.4 years; the range was nineteen to sixty-two years.

Men with anxiety neurosis (neurasthenia, neurocirculatory asthenia). Comparable observations were made in these laboratories in 99 men with anxiety neurosis (neurasthenia, neurocirculatory asthenia)[21]; the data were compared with data of patients with "hysteria."

Women with hysteria. Twenty-five women with hysteria were selected from a group of 50 for comparison with the men diagnosed "hysteria." The 25 were selected from a group of 50[20] in order to render the male and female groups comparable in age. The clinical picture of hysteria as seen in women included: lack of, or vague, chief complaint; symptoms: headaches, visual difficulties, anxious spells, abdominal pain, vomiting, dysmenorrhea, sexual frigidity, paralyses and faints; excessive hospitalizations and operations; a friendly and overtalkative manner during examination; a dramatic manner of describing their past history. The mean age was 30.2 years; the range was twenty-one to forty-four years.

Methods of Study

All patients were given a thorough medical, psychiatric and neurologic examination either at the time of this study or, in the case of the 6 veterans in the mental-hygiene clinic, at the time the diagnosis was originally made by physicians in the Veterans Administration. In addition to other thorough laboratory studies, electroencephalograms were recorded on any patient with fits, trances or amnesias.

The data for this study were recorded during a private interview on a standard questionnaire form previously described,[20, 22] comprising 106 items. [General categories and number of items in each were: *chief complaints* — 3; *symptoms* — 60; *check symptoms* — 4 (these concerned symptoms whose occurrence was considered improbable and were used as before[20] to note whether these patients responded "yes"; this was done to learn if examiners were suggesting symptoms to the patients); *personal, social, familial* — 21; *manner and attitude during examination* — 10; *operations, hospitalizations, injuries* — 4; *others* (to record important points not specified in questionnaire) — 5; *summarizing factors* — 3.] Scoring was done by standard criteria previously described.[22] The same criteria and scoring methods† were used for patient and control groups.

Summary of Results

Description of a Typical Case

In order to present a concrete clinical picture of this disorder, one representative composite case will be described.

Case Report

M. H., a 27-year-old man, entered the hospital with a chief complaint of pain in the back. While on military maneuvers in January, 1945, the patient fell a distance of about 5 feet, striking his left hip and shoulder. About an hour later he began to complain of pain in the region of the lumbar spine. A roentgenogram showed no evidence of fracture. Because of a continuing complaint of back pain, he was hospitalized in February. About this time the patient began to complain of nervousness. He felt tense, was easily upset and stated that he was disgusted about his condition. He complained that he suffered from tingling in his extremities when upset, from daily headaches (which were described as tight feelings in the forehead and back of neck), from feelings of light-headedness, from sighing and from pounding of the heart on the slightest exertion. There was no improvement in his condition. He was given sick leave from May to July. His irritability had caused some marital discord, he believed. In September, 1945, he received a medical discharge from the army with a diagnosis of conversion reaction. Since his discharge there has been no change in his condition. He receives a 40 per cent disability compensation from the Veterans Administration and has been once hospitalized in a Veterans Administration hospital for diagnosis and treatment, where a diagnosis of conversion reaction was again made. The back pain causes enough disability, he states, that he has missed about 25 per cent of working time as a civilian.

*The word hysteria, without quotation marks, will be used for the disease hysteria that occurs in women and for the condition as it is commonly described in the literature.[20] The word "hysteria," with quotation marks, will be used to refer to the special condition described in this paper and is a special usage of the word.

†Statistical calculations[23-27] were made, as previously described,[20] and checked by Mrs. Alice Kilpatrick; Mrs. Mary L. English, Miss Eleanor W. Reed and Mrs. Martha W. Altmann assisted in the preparation of the tables and manuscript.

Past history and system review yielded no relevant positive findings. Physical examination elicited no positive findings, except that he walks intermittently with a slight limp. The patient appeared irritable, tense, restless and slightly belligerent. During the examination the patient complained of the quality of the medical care he had received in the service and in the Veterans Administration hospital. Laboratory findings were within normal limits. The patient showed no improvement and his complaining persists. He works irregularly and continues to receive a pension. His medical care is complicated by his belief that some of his physicians think he is malingering.

Characteristics of "Hysteria" in Men

Age of onset. The age of patients at the onset of the first symptoms was from twelve to forty-two years; the mean age was 25.7 years. Onset was earlier than the age of eighteen in 8 per cent of the patients; it was after the age of thirty-five in another 8 per cent.

Chief complaints. Examples of chief complaints are: (Cases 1-10) pains in middle of back and stomach; sick at stomach and nervous; all nervous inside and pass out; ache in right arm and tender spot behind left ear; family worries, sick and wants to get out of radio work; pain in back and legs; pain in back; worked late, became dazed, delirious and babbling; pain in testicles; pain in legs; (Cases 11-20) tinnitus, headache and nervousness; knees hurt; pains in neck and weakness in left arm; headaches; backache; walking limited due to aches in legs and swelling in ankles; pain in base of spine, knees, neck and shoulder; can't seem to remember things and rave at night; headaches; pain in shoulder; (Cases 21-30) gone for thirty days and don't remember it, left side hurts, jumpy and almost passed out; pass out, go numb, and don't know what I'm doing; nerves and side got me, my mind stays on itself; blackouts, dizzy spells, and stomach gives out, vomits; weakness; headaches; spells; attacks when I get up from sleeping, can't get up or open eyes; pain in back; insomnia; (Cases 31-38) vomiting; lameness of shoulder and immobility of left arm; sacroiliac condition; pain in stomach, poor appetite and weight loss; pain in neck, arm, and heels, tired at end of day, not the same since injury; ruptured disk, paralyzed, leg dead, burning feeling all over, thought I was going crazy, pressure in head; vomiting, nervousness, finger and arm hurt; aching in back.

Men with "hysteria" described a specific chief complaint less frequently (76 per cent) than did the patients with chronic medical illnesses (97 per cent). The presence of a specific chief complaint obviously did not rule out "hysteria." The absence of a specific chief complaint was, however, unusual in medically ill patients.

Symptoms. Of the 41 symptoms that were systematically investigated in the patient and healthy-control groups, the average number of symptoms per patient was 11 (range, 6-21); in the healthy men, the average number of symptoms was 2.5 (range, 0-8). These differences are significant. Twenty-four of these 41 symptoms occurred with significantly higher frequency in patients than in controls (Table 1). Patients also showed 14 other symptoms more frequently, but not significantly so.

Headache, nervousness, being easily upset, dizziness, dyspnea, palpitation, paresthesias, abdominal pain, nausea and vomiting, symptoms of sexual difficulties, unexplained pains in back, joints and extremities, trances and amnesias occurred much more frequently in men with "hysteria" as compared with healthy men (Table 1). Symptoms that occurred in over half the patients were back pain, pain in extremities, headaches, dizziness, nervousness and being easily upset.

TABLE 1. *Symptoms of 38 Men with "Hysteria" Compared with Those of 39 Healthy Men.**

SYMPTOMS	PREVALENCE OF SYMPTOMS		SIGNIFICANCE† RATIO
	"HYSTERIA"	HEALTHY CONTROLS	
	%	%	
Headache	68	23	4.0
Nervousness	68	15	4.7
Easily upset	65	15	4.4
Pain in extremities	61	3	5.5
Pain in back	59	18	3.7
Dizziness	59	13	4.2
Dyspnea	47	8	3.9
Palpitation	47	10	3.6
Abdominal pain	47	26	2.0
Nausea	47	13	3.3
Paresthesias	47	3	4.6
Blurred vision	45	3	4.4
Pain in joints	42	3	4.1
Vomiting	32	5	3.0
Anxiety attacks	26	0	3.4
Depression	24	0	3.2
Anorexia	24	5	2.3
Faints	21	3	2.5
Premature ejaculation	20	0	2.8
Amnesia	19	0	2.9
Painful intercourse	17	0	2.6
Sexual indifference	16	0	2.6
No sex pleasure	14	0	2.4
Trances	13	0	2.3

*The two groups did not differ significantly in the prevalence of the following 17 symptoms (significance ratio less than 2.0 in each case): blindness (patients 5 per cent, controls, 0); diplopia (0, 0); triple vision (0, 0); lump in throat (8 per cent, 3 per cent); aphonia (6 per cent, 0); food dyscrasia (21 per cent, 8 per cent); constipation (18 per cent, 8 per cent); diarrhea (11 per cent, 3 per cent); variation in weight (18 per cent, 5 per cent); urinary retention (0, 0); impotence (9 per cent, 0); paralysis (6 per cent, 0); fits (6 per cent, 0); sleepwalking (13 per cent, 8 per cent); sleeptalking (50 per cent, 44 per cent); cry easily (13 per cent, 3 per cent); suicidal attempt (0, 0).

†Significance ratio of 2 or over represented a significant difference.

Other symptoms sometimes referred to as characteristic of hysteria[6, 7, 9, 16] occurred, but infrequently (Table 1). The finding of a low frequency of these "characteristic" symptoms may differ from popularly held medical opinions but is consistent with the data of other workers who have had wide experience in this field (Briquet, 430 cases[6]; Savill, 500 cases[9]) and agrees with statements such as those by Wechsler[16]: "Hysterical convulsions are extremely rare. . . . (Paralysis) has become a comparatively rare phenomenon in civil practice. . . . (anesthesias) while not really so common as was once believed, occasionally occur. . . ."

Manner and attitude during examination. Observations of the manner and attitudes of the patients showed that 34 per cent expressed dissatisfaction with their medical care, past or present, as

compared with 7 per cent of medical controls (significance ratio, 2.8); that 26 per cent were suspected of malingering by at least one physician as compared with none of the medical controls (significance ratio, 3.1) and that 16 per cent described their illness in an unusually dramatic or loquacious manner, as compared with none of the medical controls (significance ratio, 2.3).

In order to test a notion held by some psychiatrists that patients with hysteria look young for their age, the differences between the estimated age and the true age of patients and controls were compared. In men diagnosed "hysteria" the estimated age was on the average 1.4 years less than the true age; in the chronically ill controls, 1.2 years. This difference of 0.2 years was not statistically significant (significance ratio, 0.3); thus men diagnosed "hysteria" do not appear unusually young.

Past history: hospitalizations. In men with "hysteria" the mean number of previous hospitalizations averaged 4.1 and was significantly greater than 2.5 hospitalizations for the chronically ill controls (significance ratio, 2.8) and 1.9 hospitalizations for the healthy controls (significance ratio, 6.6). The hospitalizations were also calculated on the basis of 1000 person-years per person to allow for differences in the mean ages of the three groups. In men with "hysteria" the mean number of previous hospitalizations, 135 per 1000 person-years per person, was significantly greater than 81 in medically ill controls and 64 in healthy controls. (Significance ratios: "hysteria" *vs.* medical, 2.5; "hysteria" *vs.* healthy, 3.4). This shows that men with "hysteria" were hospitalized more frequently than were control subjects.

The men with "hysteria" had a mean of 1.6 major surgical procedures (appendectomy, spinal fusion, tonsillectomy and others) per patient — the healthy men 1.3 and the chronically ill controls 1.1. The mean number of major surgical operations was calculated per 1000 person-years per person. These averaged 54 for the patient group, 39 for the healthy controls and 35 for the chronically ill controls. These differences are not statistically significant. Only four of the 38 patients seemingly had operations as a consequence of their "hysteria"; the rest seemingly had them for definite surgical indications. "Hysteria" in men was not demonstrated to lead to excessive surgical procedures.

Personal and social history. Marital difficulties (divorce, separation or serious marital discord) were much more frequent in this group than in the healthy controls; 54 per cent in the patient group had difficulty compared with 11 per cent in the control group. Arrests occurred in 14 per cent of the patients; none were noted in controls; excessive alcoholic intake occurred in 8 per cent of the patients, as compared with none in the controls. In other aspects, the personal and social histories of the patients did not differ significantly from those of the controls.

Comparison of some symptoms of "hysteria" in men with those in anxiety neurosis (neurocirculatory asthenia, neurasthenia) (See "Discussion").

Testing the possibility of the examiners' suggesting symptoms to patients. No patient answered "yes" to any of the 4 check questions (pain in tip of left ear, pain in right big toenail, thighs turned red, hair turned white suddenly), which were included to test the possibility that the patients' symptoms might be suggested by the questioning. In addition, there were three questions on symptoms (diplopia, urinary retention and suicidal attempt) that the investigators thought would probably be answered affirmatively by some of the patients; these were nevertheless answered negatively by every patient.

The results indicated that the examiners' beliefs, possibly reflected in manner or inflection of voice in asking questions about symptoms they believed would or would not occur in "hysteria," did not necessarily suggest "yes" or "no" answers to the patient.

Comparison of "hysteria" in men with hysteria in women: age of onset of illness. The mean age of onset was 25.7 years in the men and 16.9 years in the women. This nine-year difference is statistically significant (significance ratio, 6.3), but the selected character of the male group (largely service personnel) may render the meaning of this difference uncertain.

The mean number of symptoms in men was 11, in women 20. This difference is significant (significance ratio, 7.7).

Table 2 shows that the women had more symptoms than did the men. Thirty-one symptoms of 38 occurred with greater frequency in women, 21 of these with a significantly greater frequency.

In addition, there were some symptoms, such as urinary retention, lump in throat, story of weight variation, food dyscrasias, sexual symptoms and anxiety attacks, that were characteristic of hysteria in women but were not striking in "hysteria" as seen in the men in this study.

The compensation factor was more frequent in men with "hysteria" than in women with hysteria, 100 per cent *vs.* 8 per cent (Table 3). For purposes of this study, compensation was defined as the prospect of tangible material reward accruing from the illness, such as collecting money from pension or insurance, release from military service or avoiding arrest or prosecution. No subtle, intangible or purely psychologic type of "compensation" was included in this definition. Relative frequencies of chief compensation factors are illustrated in the figure.

The men presented more specific and well defined chief complaints than did the women. In contrast, a striking feature of hysteria in women was the vague

character of the chief complaint or multiple "chief complaints."

It was striking that almost all (92 per cent) of the women related their history in a loquacious, exaggerated and dramatic fashion, which was uncommon (16 per cent) in the men. This was not entirely explicable on the basis of the commonly held male hypothesis that "women talk too much," since none of the medically ill control women[20] exhibited this dramatic loquaciousness.

Twenty-six per cent of the men were thought by at least one referring physician to be malingering, on the basis of the nature of the patient's symptoms or attitude. Nine per cent of the women were suspected of malingering. Sixty-eight per cent of the men but only 18 per cent of the women thought that they had been helped by treatment.

TABLE 2. *Statistically Significant Differences in the Frequencies of Symptoms in 38 Men with "Hysteria" and in 25 Women with Hysteria.**

SYMPTOMS	PREVALENCE OF SYMPTOMS		SIGNIFICANCE RATIO
	MEN	WOMEN	
	%	%	
Abdominal pain	47	80	2.6
Nausea	47	80	2.6
Paresthesias	47	76	2.3
Anxiety attacks	26	76	3.9
Anorexia	24	80	4.4
Depression	24	48	2.0
Faints	21	60	3.1
Food dyscrasia	21	74	4.1
Constipation	18	56	3.1
Variation in weight	18	68	4.0
Painful sexual intercourse	17	60	3.3
Sex indifference	16	83	5.2
No sex pleasure	14	75	4.5
Trances	13	44	2.8
Cries easily	13	63	4.0
Diarrhea	11	40	2.8
Lump in throat	8	71	5.2
Lose voice	6	31	2.4
Paralysis	6	36	3.0
Double vision	0	12	2.2
Urinary retention	0	42	4.3

*There were 17 symptoms in which the frequency in men did not differ significantly from that in women. In 10 of these 17 symptoms (headache, dizzy spells, dyspnea, palpitation, blurred vision, vomiting, sleepwalking, fits, blindness and suicidal attempt) the frequency was slightly higher in women than in men. In 7 of these 17 symptoms (nervousness, getting easily upset, pain in the extremities, pain in the back, sleep-talking, pain in the joints and amnesia) the frequency was slightly higher in men than in women.

The mean age of the men and women patients was the same — 30.2 years.

The women patients were not hospitalized significantly more frequently than the men patients (4.4 hospitalizations per person for the women, 4.1 for the men — difference not significant). A consideration here may be the ready availability of hospitalization for service personnel. There was only one admission to a psychiatric hospital. The mean number of non-indicated hospitalizations (for hysteria symptoms that should not have necessitated medical or surgical hospitalization) was 3.0 in the women and 1.3 in the men. The difference is statistically significant (significance ratio, 2.5).

Women patients had approximately twice as many major surgical operations as the men, a mean of 2.9 per person in the women and 1.6 in the men. The difference is statistically significant (significance ratio, 2.3). The mean number of operations for hysteria in the women was greater than for "hysteria" in the men, 1.8 per patient for the women and 0.2 per patient for the men. The difference is statistically significant (significance ratio, 4.3). It was concluded that men with "hysteria" did not have the excess of surgical operations found in women with hysteria.

Twenty-nine per cent of the women habitually took some opiate or daily doses of barbiturates; none of the men did. Forty-four per cent of the women, as compared with 5 per cent of the men, stated that their illness often caused them to miss school during childhood and adolescence. This was consistent with the later age of onset in men.

There were no apparent differences in the frequency of marital difficulties (divorce, separation or statement of serious marital discord) — men 54 per cent, women 53 per cent.

Resemblance of the symptoms of psychopathic personality to those of men diagnosed "hysteria" and women with hysteria. Six patients with psychopathic personality were examined, each presenting multiple complaints and each having at least one of the "classical" symptoms of hysteria — blindness, loss of voice, urinary retention, paralyses, fits, trances or amnesias. (These are mentioned here as a reminder that patients with psychopathic personality may have some symptoms resembling those of "hysteria.") Those patients diagnosed psychopathic personality were excluded from the "hysteria" group. The diagnosis of psychopathic personality was made on the basis of its characteristic clinical picture: civilian arrests, suicidal attempts, poor school adjustment with a history of being suspended or expelled or both, poor job history with jobs being held for only short periods, history of proved theft, chronic alcoholism and conspicuous failure

TABLE 3. *Special Features of "Hysteria" in 38 Men Compared with Those in 25 Women with Hysteria.*

	PREVALENCE		SIGNIFICANCE RATIO
	MEN	WOMEN	
	%	%	
Chief complaint			
No specific chief complaint	24	52	2.3
Compensation problems			
Any kind of compensation problem	100	8	7.4
Monetary pension problems	100	8	7.4
Out-of-service problems	55	0	4.6
Symptoms related to injury	55	0	4.6
Manner and attitude			
Dramatic description of past history and present illness	16	92	5.9
Overtalkative	16	92	5.9
Overfriendly	8	80	5.8
Accused of malingering	26	9	3.4
Helped by any treatment	68	18	3.7
Personal and social difficulties			
Frequent absences from school due to illness	5	44	3.7
Frequent absences from work due to illness	55	24	2.5
Drug habit or addiction	0	29	3.5
Unusual trouble with own children	10	67	3.3

to advance in the army. In the psychopathic-personality patients three of these symptoms occurred in 3 patients, four in 2 patients, and five in 1 patient.

Discussion

The question whether hysteria really occurs in men made it important to make studies on a series of men diagnosed hysteria. Since it is not clearly established that the disease really exists in men, it is difficult to know whom to select and where to find patients for such a study. Since no clear-cut criteria have been established for the disorder, it was necessary to start with approximate criteria that combined old concepts and present-day diagnostic schemata[6, 9, 16, 20] in searching for such patients. It was discovered, then, that for practical purposes they were found only in service hospitals, in Veterans Administration medical facilities, and rarely in civilian hospitals as patients with monetary compensation problems.

This was a revealing finding, as physician colleagues were generally certain that every civilian-hospital ward had many cases of hysteria in men, but attempts to produce such cases failed. Patients presented to the examiners as cases of hysteria included patients with cerebral embolus and aphasia, patients with tetanus, epilepsy, catatonic schizophrenia, carcinoma of the stomach, torticollis, multiple sclerosis, poliomyelitis and retrobulbar neuritis, among others.

At the same time and in the same hospital where the women with hysteria were observed, there was a constant supply of cases of anxiety neurosis in both men and women and of cases of hysteria in women.

The authors wondered whether the absence of cases of hysteria in the civilian men might have resulted from placing too many men in the undiagnosed category. The facts were that of 388 cases in the civilian psychiatric study series, 18.4 per cent of 267 women and 25.6 per cent of 121 men did not receive psychiatric diagnoses; that is, the symptoms could be explained by a definite nonpsychiatric disease or the symptoms could not be explained by any diagnosis. It can be calculated that the excess of undiagnosed men patients, proportionate to the total numbers of men and women, was 9 cases. Even if every one of these 9 patients had hysteria (and there is no evidence that they did), this would still be a remarkably low number compared with the 91 cases[20] of women with a definite diagnosis of hysteria.

The following clinical picture emerged from the study of men with hysteria. There were: special symptoms of frequent occurrence such as pains in back and abdomen (Table 1); the "characteristic" symptoms, mentioned previously; and the constant feature of a material compensation factor.

In addition, there was a set of symptoms including headaches, dizzy spells, dyspnea, palpitation and nervousness, sometimes called "anxiety" symptoms, which are common to other neuropsychiatric diseases. Many of the latter symptoms mentioned above were similar in both kind and frequency to those reported from this laboratory[21] in the commonest of the "psychiatric" diseases, anxiety neurosis (neurocirculatory asthenia, neurasthenia). Although "hysteria" in men showed many symptoms in common with this disorder, as it does with other psychiatric and medical disorders, some of its special features suggest that it is not identical with that disorder. The fact that different psychiatric illnesses have in common some of the same symptoms, such as headaches, palpitation and nervousness, does not mean that those diseases are any more identical than are all diseases that cause cough and hemoptysis.

There are major difficulties in comparing the findings of this study with those in the literature on hysteria in men. These difficulties are illustrated by the first such case reports. In 1618 Pisonis[5] first stated that hysteria occurred in men and described two cases. The first was "a fisherman" whom Pisonis "observed" in an "epileptic paroxysm" with "stertorous breathing." This patient was "freed of this the next day by a large outflow of pure water." In the other case no clinical history was given. At autopsy, "the rear part of his head was bathed in fluid. The membranes were impregnated with this water . . . and as soon as the skull was opened, a great deal of fluid poured out." Neither case could really be accepted unequivocally as a good example of hysteria or "hysteria."

No systematic tabulation of the symptoms of hysteria in men could be found. Therefore, original case reports from the literature of hysteria in men were reviewed. One hundred and fifty-four case reports were reviewed[5-7, 10-14, 29-70] (Table 4). It can be seen that the symptoms in the patients of this study resemble those in the medical literature. Twenty-six symptoms not included in the questionnaire of this study are noted in the reviewed series (Table 4). Ten of these 26 symptoms, however, were noted under "other" in the questionnaire of this study. There was a total of 645 symptoms in the 154 cases reviewed. There was a mean of 4.2 symptoms per patient; 3.2 of these symptoms were included in this study's questionnaire and 1.0 of these symptoms was not included in this study. This method of pooling all case-report data yields a picture that resembles the patients of this study in many respects. The cases in the literature differ from the cases in the study in lacking compensation factors (or, more exactly, in lacking any information, affirmative or negative, about compensation factors) and in the high proportion of fits in the cases in the literature. It should be commented that unusual types of fits that are today included in the epilepsy group were probably formerly believed to be manifestations of hysteria.

This study lacked combat casualties. However, data from 10 consecutive "hysteria" cases featuring hysterical paralyses in soldiers from danger and combat zones in Korea studied in Japan by Dodge,[70] using the same method and questionnaire described here, show that his patients had the same clinical picture as did these patients. Also, those combat cases had, as did these patients and the women with hysteria,[20] a high frequency of symptoms such as nervousness, being upset, dyspnea, palpitation and anxiety attacks — symptoms of "anxiety." This indicates that the belief that patients suffering from so-called conversion symptoms "do not at the same time experience 'anxiety' consciously" is not necessarily correct. In fact, the entire general theory expressed as "instead of being experienced consciously. . .the impulse causing the anxiety in conversion reaction is converted into functional symptoms"[71] has never been supported with adequate definition of terms and adequate correlated observations on a series of cases.

Is "hysteria" in men identical with "compensation neurosis" (also referred to as "traumatic neurosis" or "traumatic hysteria") as noted in the literature?[16-18, 72-78] This question cannot be answered finally, since the various studies are not comparable. However, as far as comparison is possible, there are many similarities between these cases and those described in the literature of "compensation neurosis." A further question arises: "Did the method of selection of men with 'hysteria' determine completely the results of this investigation?" Undoubtedly this was an influential general factor, but it did not determine the detailed findings of the study.

Another question is: "Does the illness diagnosed 'hysteria' in men have the same or a different clinical picture from hysteria in women?" The data suggest that the clinical picture in men differs from that in women. The important differences were: The illness is of later onset in the men; in all the men there was the possibility of obvious and material gain whereas in the women this was not found — it could be speculated that the women with hysteria might gain in some subtle psychologic way, but such theoretical gains were not included in the definition of material gain; the women had many more symptoms, and they presented their histories dramatically, vaguely and colorfully, as compared to the men; the men had fewer hospitalizations for misdiagnosed psychiatric reasons and had no excessive surgery.

Differences in the clinical picture in men and women suggest the question, "Is 'hysteria' in men a different disease or a milder form of the same disease that occurs in women?" This question cannot be answered finally until an objective or crucial diagnostic test for hysteria is discovered. In the meantime, on the basis of the data and calculations it seems a sound working conclusion that the two diseases are different and that true hysteria probably does not occur in men or else is extremely rare. Until the answer is clearer it is important in studies of hysteria to keep separate the data on men and on women. It would not, moreover, be unique for an illness to affect one sex predominantly. This is true of many illnesses — for example, hemophilia, coronary-artery disease, gout, eclampsia, disseminated lupus erythematosus and others.[79] If the disorder in men discussed in this paper is not really hysteria, why call it that? Should some other name from the literature be used, or should a new name be invented? The authors do not wish to persuade physicians to adopt new terminologies for hysteria nor to adopt the device "hysteria" that was necessary for clarity in this presentation. It does not seem sound to create a new terminology until facts about cause or crucial mechanisms are known.

It is the clinical impression of the authors that an illness identical with "hysteria" as diagnosed in men does occur in women when immediate and obvious material gain is associated with being ill. This "hysteria" as diagnosed in women would then also be different from hysteria in women as characterized previously in another study.[20]

TABLE 4. *Description of Hysteria in Men* in 154 Cases from the Medical Literature.*[5-7, 10-14, 38, 69]

SYMPTOMS	No.	PREVALENCE %
Fits	78	50
Headache	41	27
Paralysis	39	25
Nervousness	35	23
Abdominal pain	34	22
Dyspnea	21	14
Pain in extremities	20	13
Dizziness	19	12
Lump in throat	18	12
Aphonia	16	10
Depression	16	10
Vomiting	15	10
Pain in back	13	9
Trances	12	8
Sleepwalking	11	7
Paresthesias	11	7
Blindness	10	7
Anorexia	10	7
Palpitation	9	6
Pain in joints	9	6
Amnesias	9	6
Constipation	6	4
Easily upset	6	4
Diplopia	5	3
Weight variation	5	3
Blurred vision	4	3
Urinary retention	4	3
Faints	4	3
Cry easily	4	3
Impotence	2	1
Premature ejaculation	2	1
Diarrhea	2	1
Anxiety attacks	1	1
Food dyscrasia	1	1
Sleep-talking	1	1
Suicide attempt	1	1
Sex indifference	1	1
No sex pleasure	1	1
Nausea	1	1
Painful intercourse	0	0

*The following 26 symptoms, not included in the questionnaire of this study, were noted in the medical literature: tics and tremors, tinnitus, chest pain, cough, deafness, psychotic episode, gait disturbances, speech disturbances, hemoptysis, insomnia, nightmares, enuresis, difficulty in thinking, masturbation, polyuria, urinary incontince, fever, ear pain, belching, hiccough, yawning, gluttony, pseudocyesis, sexual perversion, dysuria and edema of extremities. There were only 2 symptoms of these 26 with a prevalence of greater than 10 per cent — tics and tremors 20 per cent and tinnitus 10 per cent. (In most of the studies cited, the *absence* of a symptom was *not* specifically noted; for purposes of calculating this table, all symptoms not mentioned were treated as absent.)

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It should be emphasized that the observations on these patients were made using the standard procedure of the general field of diagnostic medicine — eliciting chief complaint and past and present history and performing examination and relevant laboratory investigation. This study has not employed ideas or words represented by such terms as "conversion," "oedipus complex," "contraction of the field of consciousness," "repression" and "unconscious."[14, 15, 71, 80-82] Use was not made in this study of these words and ideas because they represent almost no quantitative or controlled observations and they have not proved applicable for practical clinical purposes, as previously stated.[20] The authors are aware that the study of clinical phenomena of disease (descriptive medicine) is not the optimum or final stage of study — that it is not an end in itself but represents only a step toward the ultimate understanding of disease. It does, however, represent the level of present-day knowledge of hysteria and incidentally of most of the "psychiatric" diseases. Granted that we have not really emerged from this stage, it seems better to depend on verified clinical phenomena as a basis for further progress than to act as if we possess a body of knowledge about causes and mechanisms that in fact we do not as yet possess.

This study gives no final information on the cause of "hysteria" as diagnosed in men. A consistent association is that of "hysteria" with compensation factors. Further study of this association is warranted.

Conclusions

In the study of men and women patients, it was discovered that cases of hysteria were easily found among women but not among men.

The idea that hysteria as seen in women is rare or nonexistent in men is not a new idea. It is at least 2000 years old and may be found in the writings of Hippocrates, Aretaeus, Galen and Celsus and in the more recent studies of Briquet, Savill, Mitchell and Charcot.

In order to find men diagnosed "hysteria" it was necessary for practical purposes to examine patients in service hospitals and in the Veterans Administration medical facilities. In civilian hospitals the condition was found only in patients with monetary compensation problems. The first 38 such patients located were studied in order to learn about their clinical characteristics. These characteristics differed so strikingly from those of hysteria in women that it seemed desirable to use, for purposes of this presentation, a different term for the men patients — "hysteria."

The commonest chief complaints were musculoskeletal pains, abdominal pain, nausea and vomiting or nervousness. The commonest symptoms were headache, being easily upset, giddy spells, dyspnea and palpitation, similar to those occurring in other nervous illnesses; abdominal pain; nausea and vomiting; and musculoskeletal pains. In addition, complaints included at least one of the "classical" symptoms — amnesia, blindness, fits, trances, special pains, vomiting, paralysis, impotence or aphonia. The compensation factor of possible immediate personal gain (compensation [100 per cent], discharge from army [55 per cent], avoiding punishment [5 per cent]) was present in every case. This condition occurred in patients with no previous history of ill health or of specific psychiatric disease. Characteristically, patients expressed dissatisfaction with the quality of their medical care; in turn, physicians sometimes suspected them of malingering.

"Hysteria" as diagnosed in men is probably not the same disease as hysteria in women.

The use of words such as "conversion," "unconscious," "oedipus complex," "repression" and "infantile and childhood developmental experiences" did not add to the understanding of "hysteria" or to its accurate clinical diagnosis.

The diagnosis "hysteria" in men where circumstances show no possibility of material gain (such as collecting money or avoiding military service or punishment) is probably inaccurate and necessitates searching for the correct one to avoid embarrassing or harmful errors.

For purposes of further research it seems wise at the present state of our knowledge to regard hysteria in women as a different condition from "hysteria" in men and to keep separate the data from these two groups.

Addendum. Since the completion of this manuscript 1 case that may be a case of male hysteria without an active compensation problem has been presented to the authors, although the past history includes both a successful lawsuit after an automobile injury and medical benefits from the city following a second injury. The patient is right-handed and has a history of right-sided convulsions with speechlessness following a left-sided craniotomy. In one spell of speechlessness, faradic treatment over the larynx produced immediate return of speech. If the diagnosis of hysteria is substantiated, he will represent the first civilian male noncompensation case to be seen by the authors. We would like to hear of others.

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CONDUCTION OF VISCERAL PAIN*

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ALTHOUGH our Puritan ancestors may have thought that pain was a scourge of God to try the soul of man, few modern philosophers would agree with this concept. The attempt to control chronic pain by surgery constitutes a relatively new field of medical endeavor, and most of our knowledge about it dates from the advent of local anesthesia. The only suitable experimental animal is man himself, as even our closest furry relatives cannot tell us what they feel. Furthermore, as we shall see, cats, dogs and even monkeys are poor experimental animals, since there are known differences between their pathways of pain conduction and ours. Many of the fundamental problems in our quest for knowledge concerning the physiologic mechanisms and conduction pathways of pain must therefore be settled by careful observation and experimentation on the human subject, and the unpleasantness of the experiments has deterred many investigators.

This paper outlines the development and extent of present-day knowledge concerning pain from the viscera and how every operation for its relief in co-operative patients who are good surgical risks can be expanded into an investigative procedure. The patient is fully informed of the study that has been planned; if he is apprehensive he is sedated with intravenously given Demerol or Pentothal in addition to the standard regional infiltration of procaine-adrenalin solution. With the help of expert anesthetists it is usually possible to supplement the basal sedatives with the inhalation of light concentrations of nitrous oxide, so that the patient remains unconscious until the structures to be tested and cut are fully exposed. Despite this degree of narcosis, the patient will usually awaken within ten minutes; hence the surgeon, if not pressed for time, may have a fully conscious and co-operative subject for testing. As soon as this has been completed the patient may again be put to sleep; on awakening he will rarely complain or even remember any discomfort.

The first experimental observations on man date back to Lennander's[1] paper in 1901, giving his observations on intestinal sensibility in the course of operations under local anesthesia. Lennander found no evidence of pain on cutting, burning or crushing loops of bowel. Only traction on the mesentery was painful; he ascribed this to the functioning of the terminal twigs of the spinal nerves in the posterior peritoneum and root of the mesentery.

The fundamental error of Lennander's observations lay in the fact that neither cutting nor burning nor crushing is a basic physiologic stimulus. This, as pointed out by Hertz[2] ten years later, is distention of unstriated muscle. In the case of cardiac and other muscular structures it is ischemia (Sutton and Lueth[3]). We now realize that the viscera, as well as other deep structures like skeletal muscle, require a massive stimulus because of their poor supply of pain-conducting fibers.[4] These consist of fine, beaded terminals, with nerve fibers having little or no myelin and a relatively slow rate of conduction. In the cornea, which is endowed with little sensitivity other than to pain, the beaded, undifferentiated terminals are the only type of nerve endings present. The periosteum, which has a rich supply, is the most sensitive of the deeper structures and the most capable of localizing the source of painful stimuli. In all the viscera, on the other hand, these endings are relatively sparse.

The notoriously high threshold of viscera to pain is lowered during inflammatory states, as is also true of other deep structures such as ligaments, joints and skeletal muscle. Thus Wolf and Wolff[5] have found in a patient with a gastric fistula that after application of mustard the normally insensitive mucosa can appreciate the pressure of a glass rod. In operating under abdominal-field block anesthesia, Kinsella[6] observed that compressing the walls of the inflamed appendix is distinctly painful. In experiments on dogs with Garrey and Atkins,[7] I was able to corroborate Sutton and Lueth's[3] finding that pain is invariably elicited by myocardial ischemia from temporary occlusion of the descending branch of the left coronary artery. This type of pain, as well as that from distention of various hollow viscera, is prevented by regional sympathetic denervation.

In the course of many sympathectomies Sweet and I[8] have allowed the patient to awake and have then stimulated the thoracic and lumbar ganglia and the splanchnic nerves. When stimulation is limited to their distal ramification nothing is felt, but on application of a 1- to 3-volt, 30- to 60-cycle current to the central cut end of a splanchnic nerve, pain is experienced deep in the chest or abdomen. It resembles the ill defined ache of visceral colic.

It is therefore evident that internal organs have definite sensitivity to pain, but the threshold is high and localization poor. The work of the Oxford anatomists, summarized by Weddell,[9] shows that ability to localize the source of a stimulus depends on the richness and overlapping of sensory terminals. The accuracy of stimulus localization is related to the density of innervation. In the skin, the mucosa of the bodily orifices, the cornea and

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the periosteum, the rich supply of beaded pain endings is in striking contrast to the sparsity of these terminals in visceral structures. Consequently, it is not surprising that the visceral pain threshold is high and that the ability to localize its source is poor. In addition, man fortunately has comparatively little experience with visceral pain and does not build up an elaborate cortical projective pattern of the interior of his body. In the newborn infant the same is at first true of superficial sensation. It is only when the baby has seen and experienced the exact source of painful stimuli to its integument that accurate localization by the cortex becomes possible. Another reason that visceral pain is so poorly defined and consists only in a dull aching quality is that these deep structures have none of the differentiated nerve endings that are capable of appreciating temperature or touch. These are responsible for the rich overtones of cutaneous pain evoked by superficial pricks, bruises or thermal stimuli. These factors give a satisfactory explanation for the quantitative differences between cutaneous sensibility and that of deeper structures. The over-all similarity between sensations arising in skeletal muscles, fasciae and ligaments and in the viscera has been emphasized by Lewis[10] in his monograph *Pain*. Furthermore, he demonstrated that in a person suffering from angina pectoris or abdominal colic exactly similar pain is induced by injection of hypertonic saline solution into the spinal ligaments or deep fascia supplied by the same spinal nerves.

Experience with cardiac and splanchnic denervation in man, as well as direct stimulation of these nerves, has shown that the sympathetic trunks to the thoracic and abdominal viscera all carry afferent fibers. A large proportion of the axons in the splanchnic nerves have the typical histologic characteristics of sensory fibers (Kuntz[11]). Because these all enter the central nervous system over posterior spinal roots, they should not, properly speaking, be called sympathetic fibers. The autonomic nervous system, by definition of Gaskell, Langley and Cannon, consists of motor nerves to smooth muscle and glandular structures. Its principal trunks, however, are mixed nerves containing motor fibers that control sweating and hair erection in the skin and vasomotor and visceral activity throughout the body, as well as the afferent pain-conducting fibers from the internal organs.

In contrast to the importance of the sympathetic cardiac and splanchnic nerves in transmitting pain from the heart and abdominal viscera, the vagi carry visceral sensation only from the trachea, main bronchi and esophagus. B. Cannon[12] was unable to elicit any evidence of discomfort in cats on stimulating the abdominal vagi with buried electrodes; this has been corroborated in man through direct stimulation at operation by Grimson and his associates.[13] Leriche[14] also stimulated the vagus under local anesthesia in the course of stellectomy for angina pectoris. This evoked no response, but when the electrode was applied to the stellate ganglion the patient complained of typical anginal pain. More recently, however, Morton, Klassen and Curtis[15] have shown that tracheobronchial irritation in carcinoma of the lung is relieved by cutting the vagi below their recurrent laryngeal branches. When this has been performed on one side, electrical stimulation of the bronchial walls is no longer painful on the denervated side but elicits painful responses on the control side on which the vagus is intact. Sensation from the esophagus is also probably transmitted over the vagi, as Jones and Chapman[16] found that distention of its lower portion with a balloon was distinctly felt by patients after extensive thoracic sympathectomies, bilateral anterolateral cordotomy with high thoracic levels of analgesia and transection of the spinal cord in the midcervical region, which must have interrupted the thoracolumbar sympathetic outflow as well as the thoracic spinal nerves. From more recent tests with balloon distention by Chapman (Moore and others[17]) it is evident that sensory fibers must run upward some distance in the wall of the esophagus before joining the main vagal trunks, as distention of its lower portion still causes discomfort in patients after the standard lower-thoracic section of both vagi that is carried out in the treatment of resistant peptic ulcers.

In addition to the role of the parasympathetic vagal fibers discussed above, the sacral parasympathetic fibers are of great importance in the propagation of pain in pelvic disease. Although interruption of the sympathetic superior hypogastric plexus (presacral neurectomy) is an effective means of relieving pain from the uterine fundus in idiopathic dysmenorrhea, it has no influence on pain from the uterine cervix, prostate, bladder or rectum. Stimulation of the cervix or distention of the bladder or rectum still produces characteristic discomfort, which is completely eliminated by sacral block or interruption by disease or injury of the lower sacral nerves.[18] As reflex arcs over the second, third and fourth sacral roots must be left intact to preserve control of urination and defecation, it is not feasible to relieve pain from the bladder and rectum by regional sensory denervation of these structures.

We may justifiably conclude that all the viscera are sensitive to suitable stimuli and that, with the exception of the pelvic organs, the bronchial tree and the esophagus, the afferent fibers run with the sympathetic motor axons in all the visceral nerves. Both groups of fibers pass through white rami communicantes to join the spinal nerves, but those conducting visceral sensation enter the posterior roots. At this point they intermingle with somatic afferent fibers from the skin and bodily parietes, the pain-conducting axons from each

group decussating to the opposite anterolateral quadrant and ascending in it to the thalamus.

It has often been claimed that the sympathetic fibers are an accessory system for conducting pain in certain poorly understood forms of neuralgia of the head and extremities. This explanation has been invoked in migraine, atypical facial neuralgias that fail to respond to retrogasserian neurectomy, causalgia, and various types of amputation-stump pain. It is true that the pain of causalgia of the posttraumatic dystrophies such as Sudeck's atrophy and of many digital amputations associated with vasospasm and hyperhidrosis often responds in dramatic fashion to sympathectomy, but this appears to be an effect secondary to improvement of circulation and possibly, in causalgia, to a short-circuiting of efferent sympathetic impulses to the afferent somatic nerves in the brachial and lumbosacral plexuses (Doupe, Cullen and Chance[19]; Granit, Leksell and Skoglund[20]). To ascertain whether the chain of sympathetic ganglia carries pain from the arm or leg, we have on numerous occasions stimulated these structures in the course of operation, and also three times by means of pull-out electrodes placed by Simeone[21] on the lumbar chain in the course of operations on the kidney. Such stimulation has produced only diffuse discomfort deep in the abdomen or pelvis or in the back or precordium. Only in causalgia have we (and also Walker and Nulson[22]) encountered brachial radiation, presumably due to the mechanism postulated by Doupe and his associates.

Let us now return to the typical pain of visceral disease that is chronic, unbearably severe and incurable by direct surgical treatment of the diseased structures. In the case of the heart, aorta and upper-abdominal organs, as well as the kidney, ureters and uterine fundus, pain can be interrupted most safely and effectively by specific sympathetic denervation. It is outside the scope of this paper to consider details, which have been described elsewhere.[18] Experience has taught that lasting relief is nearly certain, provided that the source of pain is confined within the capsule of the diseased viscus. Thus cardiac pain from myocardial ischemia referred to the precordium and arms nearly always responds to upper-thoracic sympathetic ganglionectomy. However, when the disease is no longer confined to an organ and has invaded somatic nerves in the posterior abdominal wall, as is the case in the various forms of abdominal cancer, the surgeon must interrupt both the visceral and the somatic spinal nerves. This more extensive sensory denervation is best carried out by interruption of the secondary pain-conducting axons in the anterolateral quadrant of the spinal cord.

Former concepts of the central-spinal pathways of visceral pain are of interest because of the misleading results of animal experiments. Davis, Hart and Crain,[23] who produced biliary pain in dogs by distention of the gall bladder, observed that even staggered hemisections of the cord failed to relieve it. They concluded that afferent visceral impulses ascend bilaterally in the spinal cord with frequent cross-overs from one side to the other. Ranson,[24] in his textbook of neurology, therefore made the statement that when the spinothalamic tract is cut only on one side the analgesia of the opposite side of the body "involves the skin, muscles, fasciae, tendons, and bones, but not the viscera."

We have found that this is fortunately not true in man. A patient with chronic postcholecystectomy pain has remained free of his former pain for many years after undergoing a left-sided section of his spinothalamic tract. After anterolateral cordotomy we have tested the response to various forms of painful visceral stimuli. Distention of the renal pelvis is no longer felt on the analgesic side on injection of twice the volume of fluid that can be tolerated on the normal side, and balloon distention of the upper small intestine can also be felt only on the side ipsilateral to the cordotomy, on which the pain-conducting axons remain intact. Cutting the posterior (sensory) spinal roots is also an effective method of relieving visceral pain when it enters the cord over a small number of spinal segments, as is the case in angina pectoris and aortic aneurysm.[18]

From these observations it becomes evident that pain in otherwise intractable visceral disease can be relieved by regional interruption of visceral nerves; section of appropriate posterior spinal roots; and anterolateral cordotomy. Except in incurable disease of the trachea, bronchi, esophagus, bladder, rectum, uterine cervix and prostate, resection of the regional sympathetic ganglia and splanchnic nerves, being the simplest and safest method, is the procedure of choice unless inflammatory or malignant disease has spread beyond the visceral capsule into territory supplied by somatic spinal nerves.

Stimulation of visceral nerves in fully conscious patients and our experience with nearly 200 operations for visceral pain have confirmed the validity of these principles and corrected past errors derived from experiments in lower animals. The concept that there is no actual qualitative but only a quantitative difference between visceral and somatic pain was attacked by Mackenzie and his followers on the basis of peculiarities in reference of visceral sensation. In the light of present-day knowledge, past theories of the phenomena of referred pain require complete re-evaluation. If there is direct central conduction of visceral afferent impulses from a diseased organ like the heart or ureter, why should pain be referred to the inner aspect of the arm or to the groin? Mackenzie[25] postulated that there is no direct conduction of visceral pain to the thalamus and cerebral cortex but that impulses from a diseased viscus bombard the posterior horn of gray matter and there set up an irritable focus, so that normal subthreshold cutaneous impulses break

across the synapse to the secondary sensory neurons, which traverse the spinothalamic tract and give rise to the sensation of superficial pain. Expressed in modern physiologic terms, Mackenzie's concept of an irritable focus means that visceral stimuli facilitate somatic cutaneous impulses sufficiently to excite the production of a painful discharge in the secondary cutaneous neurons of the spinothalamic tract. Five years prior to Mackenzie's earliest paper, the theory of referred segmental pain was used by James Ross of Manchester in 1888[26] to explain cutaneous reference, but Ross thought that visceral pain had a direct "splanchnic" component as well, consisting of a deep, poorly localized ache near the midline in the substernal, epigastric or abdominal region. Head, Rivers, and Sherren[27] also arrived at the conclusion that the viscera are endowed with sensation of their own.

It is unfortunate that because of Mackenzie's more prolific writings Ross's truer interpretation should have fallen into oblivion. If Mackenzie's theory were the entire explanation, procaine infiltration of the cutaneous surface to which visceral pain is referred should relieve it. This is often not the case, as Lewis[10] "failed to alter, in the least, anginal pain in an eminently suitable patient in whom the referred pain was focused over the sternum and could be provoked, with regularity and by a constant amount of effort, both before and after thoroughly anaesthetising the affected part of the body wall." Even more devastating to Mackenzie's assumption that pain impulses reaching the sensorium come from the area to which visceral pain is referred is the observation that cardiac pain has been referred to a phantom arm after amputation (Cohen and Jones[28]).

Further evidence along this line has been given by a number of observers, who have stimulated other deep structures and various viscera and found that pain was still present after infiltration of procaine into the entire area of reference — in the shoulder area on direct stimulation of phrenic nerve (Woollard, Roberts and Carmichael[29]); in the loin and groin with ureteral distention (McLellan and Goodell[30])*; in the abdominal wall on distention of the duodenum (Wolf, Wolff and Goodell[31]). Although referred cutaneous pain and hyperalgesia can under certain conditions be relieved by local infiltration of procaine, as has been demonstrated in the original observations of Weiss and Davis,[32] it always spreads to the periphery of the insensitive area if the stimulus is increased.

In animal experiments Davis, Hart and Crain[23] found that pain produced by experimental distention of the gall bladder, although relieved by splanchnicectomy or posterior rhizotomy, is not interrupted by cutting the corresponding intercostal nerves (distal to the origin of the sympathetic rami) and the ensuing anesthesia of the lower-thoracic and abdominal parietes. White, Garrey and Atkins[7] found the same to be true of experimentally produced cardiac pain in dogs, which is relieved by resection of the four superior thoracic ganglia or upper five pairs of posterior spinal roots but is not altered if the corresponding intercostal nerves are severed.

Theobald,[33] who has given an excellent review of this controversial subject, has added some pertinent evidence from faradic stimulation of the uterine cervix and fundus of healthy women in the course of routine pelvic examinations. The referred suprapubic pain from minimal stimuli was relieved by intracutaneous infiltration of physiologic saline solution and that produced by a somewhat stronger current by 1 per cent procaine, but more intense stimulation always caused pain to break through within the anesthetic zone. Therefore it seems probable that subthreshold cutaneous afferent impulses, which enter a common spinal segment into which an irritated viscus is also discharging, may be necessary to produce awareness of mild degrees of visceral sensation. However, as soon as noxious stimulation of the viscus becomes more intense the impulses will break through to the conscious level, even if the superficial somatic innervation is blocked. Because of the paucity of nerve endings in the viscera and other deep structures and also through lack of experience of conscious sensation arising from these areas, the patient is likely to misinterpret the source of such impulses.

An alternative explanation of the central misrepresentation of painful impulses that reach the spinal cord from visceral or deep somatic structures and are erroneously referred to the skin has been proposed by Ruch.[34] This accounts for most of the phenomena of referred pain on the basis of convergence of visceral and cutaneous afferents on the same spinothalamic neurons shared by both sets of fibers. As there are many more pain fibers in the posterior roots than axons in the spinothalamic tracts, both a visceral and a cutaneous pain fiber may converge on many of the secondary neuron cells in the posterior spinal horn. On most occasions "when these particular spinothalamic neurons have been activated, stimulation of the body surface was responsible, as verified by other senses. Thus when impulses of visceral origin reach the cerebral cortex, the interpretation is made which experience has built up — that of pain arising from cutaneous pain neurons."

Further details concerning the critical data on which the theories of referred pain are based may be found in Wolff and Hardy's article "On the Nature of Pain."[35] They have divided the neurophysiologic mechanisms that underlie the perception of pain from deep tissues into three categories:

1. *True visceral and deep somatic pain.* Such pain is felt at the site of primary stimulation and may or may not be associated with referred pain. It is eliminated by in-

*According to Dr. Harold G. Wolff (personal communication), these investigators in further experiments have found it impossible to relieve the pain of distention of the renal pelvis by infiltrating procaine into the cutaneous areas of reference.

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filtration of procaine into the site of noxious stimulation or by blocking its afferent nerves, but it is not altered by infiltration of procaine into other structures supplied by the same or adjacent neural segments.

2. *Referred pain.* Such pain may occur in addition to or in the absence of the true visceral and deep somatic pain described above. It is experienced at a site other than that of stimulation but in tissues supplied by the same or adjacent neural segments. It may occur either with or without associated hyperalgesia and hyperaesthesia.

a. *Without superficial and/or deep hyperalgesia.* In this case pain depends only on the central effects of the spread of excitation of the original noxious impulses to the same and adjacent segments of the cord whence they are relayed to higher centres for perception and interpretation. Injection of procaine into superficial or deep regions of referred pain does not reduce the intensity of pain due to this mechanism.

b. *With superficial and/or deep hyperalgesia.* Referred pain may be accentuated in intensity by virtue of the effects of ordinarily non-noxious stimuli from zones of reference. Impulses from such sources, normally inadequate to produce pain, may do so upon reaching the cord in a segment involved in central spread of excitation. Procaine injected into superficial or deep hyperalgesic structures will abolish this element of the referred pain phenomenon, resulting in more or less reduction of the subject's discomfort, depending upon the amount of hyperalgesia.

3. *Pains due to secondary skeletal muscular contractions which provide a fresh source of noxious impulses.* Pain may result from secondary effects of the central spread of excitation on the effector structures, including painful contractions of skeletal muscles. Such disturbances may be widespread and the pains may be experienced in situations remote from the original source of noxious stimuli. Local infiltration of the contracted muscles with procaine abolishes this type of pain by disrupting its peripheral mechanism.

As Wolff and Hardy's experiments have so clearly shown, the most effective method of interrupting visceral pain is to interrupt the splanchnic pathways over which the primary impulses reach the central nervous system.

Surgeons who have studied the problem of visceral sensitivity from the more direct aspect of its interruption by denervation have found that after splanchnicectomy no pain can be induced by acute duodenal distention (Bentley and Smithwick[36]) or by a great variety of stimuli applied to the gall bladder and various portions of the upper intestinal tract (Ray and Neill[37]). The most convincing proof of direct conduction of visceral pain in man has recently been supplied by Bentley.[38] In the course of laparotomies for chronic peptic ulcers under abdominal-field block anesthesia he observed that the stomach or duodenal wall involved in the ulcer was directly sensitive to pressure, to needle-prick and to chemical stimulation. This disappeared after splanchnic block.

Morley[39] has also returned to a recognition of the concept of true visceral or "splanchnic" sensation, but he ascribes referred pain to local inflammatory irritation of the sensitive area of the parietal peritoneum. In this way an attack of acute appendicitis first results in midabdominal colicky pain, transmitted directly over the splanchnic nerves during the period of distention and stretching of the appendiceal wall. Later, as inflammation spreads from the organ itself to the more sensitive parietal peritoneum, it evokes pain in the right lower quadrant carried over the lower intercostal nerves. Morley's hypothesis of a "peritoneo-cutaneous reflex" undoubtedly gives a valid explanation for certain types of referred pain in visceral disease of inflammatory origin, but it fails to account for pain referred to the surface of the body in noninflammatory conditions such as angina pectoris or ureteral colic during the passage of a stone. There is no cogent reason for assuming that such a deep-lying structure as the heart, which in the course of an anginal attack neither comes in contact with sensitive parietal pleura nor undergoes any inflammatory change, can give rise to referred pain by such a mechanism. Despite Morley's helpful suggestion, we must still explain many forms of pain referred to distant areas lateral to the midline either on the basis of central misrepresentation of their source or to a viscerocutaneous reflex. After weighing the evidence I have come to the conclusion that it is not possible to discard the theory of the potentiation of visceral pain by cutaneous impulses altogether, but it is certain that this mechanism is of less importance than was formerly supposed. It has no practical application to securing permanent relief of pain in visceral disease.

Conclusions

On the basis of the evidence reviewed above, it is obvious that there are no characteristic features of visceral pain that set it apart from pain arising in deep somatic structures. Even in such a common experience as a toothache, pain often cannot be localized in the infected tooth and may even spread to other divisions of the trigeminal nerve. The phenomena of referred pain are not limited exclusively to the internal organs, and the imperfect localization of visceral pain is not related to any unique peculiarity of the viscerosensory innervation. From the surgeon's practical point of view, experience has demonstrated that it is now usually possible to obtain better results, for the control of pain, from neurosurgical interruption of the pathways that conduct visceral pain than in many of the somatic neuralgias.

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CHRONIC ULCERATIVE COLITIS AND PREGNANCY

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THE physician who is caring for the female patient with chronic ulcerative colitis is occasionally asked about the advisability of childbearing. Again, he may have the problem of treating a pregnant patient with colitis and must prognosticate concerning the effect on the mother and fetus. There is relatively little information on this subject, and the opinions expressed are conflicting.[1-6]

The purpose of this report has been to review those cases of ulcerative colitis and pregnancy that have been encountered at the Lahey Clinic. Only those cases have been considered in which adequate follow-up information and sufficient data concerning the effect of pregnancy on the colitis were available. We are aware that the group is small, but it is hoped that by stimulating interest in this phase of ulcerative colitis others will review their experience until sufficient numbers of patients have been considered to be of help in handling these cases.

CASE MATERIAL

A group of 16 patients who have answered a detailed questionnaire about the course of their pregnancy and who were seen before, during or after their pregnancies forms the basis of this report.

In all these patients the diagnosis of chronic ulcerative colitis was made by proctoscopy and barium-enema examination of the colon. In none was a specific etiologic agent demonstrated. All but 1 of the patients have been followed to the present time, the average follow-up period being eight years and seven months, the shortest three months and the longest sixteen years. Eleven patients became pregnant after the onset of colitis, with a total of 22 pregnancies, 19 viable children, including 1 set of twins, and 1 infant death. There were 2 therapeutic abortions performed elsewhere and 1 miscarriage not related to the colitis.

In 5 patients colitis developed during pregnancy. There was a total of 3 viable deliveries in 1 patient and 1 viable delivery each in 2 other patients. One fetal death and one spontaneous abortion occurred in 1 patient, and 1 miscarriage was associated with a maternal fatality.

These 16 cases have been divided into three groups: 8 patients who had mild or moderately active symptoms at the onset of pregnancy, 3 patients who were in remission at the onset of pregnancy and 5 patients in whom colitis developed during pregnancy. We have not observed an instance of pregnancy occurring in a patient who had acutely toxic and fulminating ulcerative colitis.

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Patients with Active Colitis at the Onset of Pregnancy

Eight patients became pregnant when their colitis was mild or moderately active. In these 8 patients there were 18 pregnancies, with 16 viable children, 1 pair of twins and 1 fetal death, which seemed unrelated to the ulcerative colitis. There were 2 abortions, 1 therapeutic and 1 that was spontaneous and was unrelated to the colitis. Considering each pregnancy separately, there were 6 pregnancies during which the colitis was improved. There were 9 pregnancies in which the colitis was worse after parturition, although in 2 of these the exacerbation seemed to be related to the death of the infant and in the other seemed unrelated to the pregnancy. There were 3 pregnancies that seemed to have no effect on the colitis.

From the patient's point of view, 4 thought that the colitis was improved by pregnancy, 3 thought that their colitis was definitely aggravated during and after pregnancy and 1 patient thought that the pregnancy had no effect on the colitis. The colitis became much more severe in only 2 of the entire group of patients. One patient died a year later from a transfusion reaction while being prepared for an ileostomy. The other patient, because of her present condition, will probably undergo ileostomy.

Of the 16 children, all were normal and 2 were premature. There was 1 set of twins. One child had a capillary hemangioma of the face, the only reported abnormality. The average birth weight of these children was 6 pounds, 6 ounces, which is below the normal average birth weight.

If the involvement of the colon is considered in relation to the effect of pregnancy in these 8 patients, it is seen that of the 4 patients whose disease was confined primarily to the rectum and sigmoid, 2 were worse and 2 were improved. Of the 3 patients in whom the entire colon was involved, 2 were worse and 1 was improved. In the 1 case of segmental colitis there was improvement.

In direct answer to the question "Do you believe that pregnancy is desirable for a patient with colitis?" all but 1 of these patients answered "Yes." All but 2 thought that the extra work and responsibility of a family tended to aggravate their symptoms.

Patients with Inactive Colitis at Onset of Pregnancy

Three patients became pregnant at a time when their colitis was inactive. In these patients there were 4 pregnancies, with 3 normal children, including 1 premature infant and 1 therapeutic abortion. Two patients thought that the pregnancy had no effect on their condition; 1 patient believed that the symptoms were aggravated. This latter patient was the only one who answered "No" to the question of the desirability of pregnancy. The 1 patient who had a therapeutic abortion was asymptomatic before and after this procedure. The average birth weight of these 3 viable children was 5 pounds, 10 ounces. There were no abnormalities.

If one combines these 3 patients with the 3 patients in the first group with moderately active colitis, who in the course of their disease had remissions and then became pregnant (second or third pregnancy), it may be seen that in a total of 6 patients whose colitis was inactive at the beginning of one of their pregnancies there were 3 patients who thought that the pregnancy had no effect on the colitis. One patient thought that pregnancy improved the state of the colitis, and 2 patients believed that the colitis was aggravated by pregnancy.

Combining the two groups (6 patients with inactive colitis at the onset of pregnancy), there were 3 patients whose disease was limited primarily to the rectum and sigmoid. One patient thought that pregnancy aggravated the condition, another that the process was better and the third patient that it had little effect on the colitis. In the 3 other patients in whom the entire colon was involved, 2 believed that the pregnancy had no effect and 1 that it made the colitis definitely worse.

Patients Developing Colitis During Pregnancy

Five patients who developed colitis during the course of pregnancy were acutely ill. One of the patients required an ileostomy as a life-saving measure two months after delivery of a viable child. Two patients have continued to have moderately to severely active colitis. An associated rheumatoid arthritis has developed in one of these patients; she is now in remission induced by ACTH. The other patient was having moderate symptoms when last seen. Her first pregnancy resulted in a fetal death shortly after delivery. The second pregnancy resulted in a spontaneous abortion. In 1 patient whose pregnancy was carried to term and the baby was normal, the disease eventually became quiescent. She has since had 2 children and is pregnant for a fourth time, with only minimal difficulty.

One patient died as a direct result of her disease during the sixth month of pregnancy after having a miscarriage. In all these patients the entire colon was involved.

Discussion

The described effect of pregnancy on the normal gastrointestinal tract is one of hyperirritability during the early months, followed later by some constipation. It is interesting to observe that in some of the patients with colitis in whom symptoms appeared the symptoms were worse during the first trimester, improved during gestation and were aggravated after delivery. Since this pattern is not characteristic or consistent, it indicates that

some factors other than the exaggeration of normal responses are responsible. Since ulcerative colitis is a disease of unknown etiology with an extremely variable course, it is difficult, if not impossible, to predict with any degree of accuracy the effect of pregnancy on the individual patient.

Bargen, Nunez and Mussey[1] suggested that in these cases we are dealing with a different form of colitis, or that the variability of response might be associated with some product of metabolism that was present in variable amounts, the aggravation noted possibly being the result of a foreign-body reaction evoked by this product. Other possibilities they offered were the effects of the dislocation of various hormone levels, absorption of toxic agents or overwhelming infection.

In more recent years the emphasis in chronic ulcerative colitis has been laid on the psychogenic factors.[7-10] There is no doubt that in those cases in which these influences have been adequately studied there have been striking examples of more than casual relation between psychic trauma and the onset of disease.

There are isolated case studies in which ulcerative colitis was thought to be precipitated by an unwanted pregnancy. We attempted to ascertain some of these factors in our questionnaire but, as expected, the results were not very helpful. Only one patient stated that pregnancy was undesirable in the presence of ulcerative colitis. She was an immature person whose complaints had always been out of proportion to objective findings. There was no evidence from examination that the disease process had increased in extent or severity after pregnancy. Those patients who thought that the increased responsibility of parenthood had aggravated their disease showed no more progression of the process than those who thought otherwise. It is not to be inferred that we do not consider these factors important, but they can better be elicited before pregnancy than in retrospect from perusal of records and by questionnaire. It is certainly possible that the crux of the problem of ulcerative colitis and pregnancy may be found through the proper evaluation of emotional factors.

Although many questions are as yet unanswered, we believe that this study has indicated some general trends that may be of aid in advising and caring for these patients.

The majority of patients who became pregnant when the colitis was quiescent had minimal difficulties. Those patients in whom there was reactivation were able to carry the pregnancy to term. Three of the 4 patients who have had the most pregnancies (3 pregnancies each) are at present in remission. The fourth patient, although now seriously ill, had very short intervals between pregnancies, and there was extensive involvement of the colon.

In those patients in whom there was some activity of the colitis at the onset of pregnancy, the results have been so variable that we have not been able to isolate any one factor that we thought was of real value in prognosticating the outcome. Some patients had a remarkable salutary reaction; others became worse. The extent and degree of involvement of the colon seemed to be of some significance in the severity of the reaction. We do not believe that there is any striking evidence to indicate that a patient should be advised against pregnancy. Rather, it would seem expedient to suggest delay in conception until the process becomes quiescent and to allow an adequate readjustment period of at least a year before a second pregnancy is attempted.

In regard to the effect of the disease on the fetus, aside from the less than average birth weight there is no indication that abnormalities or mortality were increased, the exception being those patients in whom colitis developed during pregnancy.

Therapeutic abortions do not seem warranted, although there are individual circumstances that might justify this decision. There is no evidence from analysis of these cases that this procedure modified the course of the disease, and there is a distinct possibility that as the pregnancy progresses the colitis will subside. The psychic trauma and frustration of therapeutic abortion in a patient who desired the pregnancy could aggravate rather than alleviate.

In our limited experience with ulcerative colitis beginning during pregnancy, it has been found to be a particularly virulent disease that responds poorly to medical treatment and can be fatal. The viciousness of the disease is similar to 3 cases reported by Tumen and Cohn.[6] Under these circumstances we believe that these patients should be under constant medical supervision and that early ileostomy should be seriously considered. There is no evidence in our cases that spontaneous abortion improved the situation, although the removal of the extra drain of the fetus on an overtaxed and acutely ill patient might be of help. It is interesting to observe that in the patient whose disease became quiescent 3 pregnancies have occurred with minimal difficulty.

An answer to the question about the advisability of pregnancy should be preceded by a sympathetic exploration of the patient's real attitude. The question may be the result of pressure from the husband or a desire on the part of the patient to be assured that she cannot have children rather than a sincere wish to be a mother. The reassuring emotional support of an understanding physician is recognized as one of the important factors in the treatment of ulcerative colitis. When pregnancy occurs regardless of physical factors this reassurance becomes even more important.

Summary

The effect of pregnancy on 16 patients with chronic ulcerative colitis has been described. Eight of the 16 patients became pregnant while the colitis was moderately active. In these 8 patients there were 18 pregnancies with 16 viable children (1 pair of twins), 1 fetal death that seemed unrelated to the ulcerative colitis, 1 therapeutic abortion and 1 abortion that was spontaneous and unrelated to the colitis. Four patients thought that pregnancy improved the colitis, 3 thought that the colitis was definitely aggravated during and after pregnancy and 1 said that pregnancy had no effect. In 1 of these patients death occurred one year later as an indirect result of the disease.

In 3 patients who became pregnant at a time when their colitis was inactive, there were 4 pregnancies with 3 viable children and 1 therapeutic abortion. Of these 3 patients, 2 thought that pregnancy had no effect on their condition and 1 believed that her symptoms were aggravated.

Five patients who developed ulcerative colitis during the course of pregnancy were acutely ill. In 3 cases viable infants were delivered. In 1 patient the process became quiescent, and she has since had 2 children and is now pregnant for a third time. One patient died shortly after a miscarriage at the sixth month. One patient had 2 pregnancies but no viable children; her last pregnancy resulted in spontaneous abortion at the third month. In the other 2 patients the disease has continued to be active; 1 required ileostomy two months after delivery and the other has developed rheumatoid arthritis.

Pregnancy that occurs during an inactive stage of ulcerative colitis is usually well tolerated. Pregnancy in a patient who is having mild and moderately active symptoms may produce variable effects. In some patients there is marked improvement; in others there is definite aggravation. If possible, pregnancy should be delayed until the colitis is quiescent, but in the majority of our patients, once it occurred, regardless of symptoms, the pregnancy was carried to term with viable children.

Ulcerative colitis that develops during pregnancy is an extremely virulent disease and may be fatal.

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RUPTURE OF THE UTERUS DURING PITOCIN INFUSION*

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INFUSION of a dilute solution of pitocin for induction of labor and treatment of uterine inertia is gaining popularity. The purpose of this paper is to report two accidents that occurred in more than 150 such cases on the Tulane Service of the Charity Hospital, New Orleans. One of these cases was previously reported in an account of our experiences with these infusions.¶

A number of precautions have evolved from our use of pitocin infusions. In the preparation of the infusion not more than 10 minims of pitocin (often only 5) is added to a 1000-cc. set. The venoclysis is running smoothly before the pitocin is added to the flask in order to prevent a large initial dose during the period of venipuncture, stabilizing of the needle and regulation of flow. The drug is administered very slowly, never more than ½ minim in any thirty minutes, and even more cautiously in the first thirty minutes. An experienced physician is in constant attendance. He observes the rate of infusion, blood pressure, fetal heart tones and the intervals, duration and intensity of the contractions. The infusion is discontinued immediately if the contractions become unduly long or intense. There is probably an increased risk of uterine rupture in women whose membranes have been ruptured a long time and in those who have had a large number of babies. Pitocin is not used in the presence of disproportion or of abnormal fetal presentation.

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Case Reports

CASE 1. A multipara with a dead fetus was at term and not in labor. In a period of 2½ hours she received 7½ minims of pitocin as an infusion. Only weak and irregular contractions were produced. She complained suddenly of lower-abdominal pain, and bright-red bleeding appeared. Instead of increased dilatation, a rupture of the lower uterine segment was found. A subtotal hysterectomy was performed. The only error recognized was the too rapid administration of the pitocin.

CASE 2. A pitocin infusion was started in a hypertensive woman who was near term. She was a multipara who had recently experienced several hours of painful contractions without increase in dilatation or effacement. A medical student was constantly at her bedside. A sudden, heavy increase of deliveries permitted only occasional observation of the patient by a resident. Three hours after the onset of the infusion the uterus was contracting very hard every 2 to 4 minutes, each contraction lasting 45 to 75 seconds. She was permitted to have this type of contraction for 2 hours, after which she suddenly began to bleed and delivered immediately. Rupture of the lower uterine segment was found and a total hysterectomy was performed. She had received only 3 minims of pitocin in 5 hours. This case illustrates the importance of having an experienced physician in attendance while the infusion is in progress. Such an attendant would have recognized that these contractions were dangerous for mother and baby and would have stopped the infusion. We know that in some hospitals this duty has been relegated to nurses and maids and in other instances the infusions have been allowed to flow unsupervised. We have found that frequently it is not necessary to continue the infusion after regular contractions have been established.

We have not discontinued the use of pitocin infusion because of these accidents. We believe that with the exercise of proper control pitocin can be used safely as well as effectively. In the management of prolonged labor due to weak and inefficient uterine contractions it has great merit. Particularly in the presence of a favorable cervix, pitocin in this form has been a dependable agent for inducing labor. When it fails nothing has been lost except a little time; other methods of effecting labor and delivery remain and have not been made more hazardous. Reports of successful experiences with pitocin drip are multiplying, but these are the first cases of rupture of the uterus following this medication.

MEDICAL PROGRESS

THE SIGNIFICANCE OF CHOLESTEROL IN THE PATHOGENESIS OF VASCULAR LESIONS*

A Discussion of the Intracellular Accumulation of Cholesterol in the Intima and of the Extracellular Precipitation of Cholesterol in the Arterial Tissue

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IT SEEMS appropriate to recapitulate briefly our present knowledge of cholesterol metabolism before we discuss a possible connection of cholesterol with vascular disease.

Cholesterol is supplied for the organism by food (exogenous quota) and by synthesis in the body itself (endogenous quota).

SYNTHESIS

We know from the experiments of Bloch[1] that cholesterol is synthesized in the organism from metabolites of low-carbon chains, especially from acetic acid. Acetic acid may be derived not only from fat but also from carbohydrate and protein disintegration. It is evident, therefore, that the synthesis of cholesterol cannot be prevented by restriction of any kind of foodstuffs. It is probable that every growing cell is capable of synthesizing cholesterol. In the mature organism the possibility of synthesizing cholesterol seems to be maintained to a higher degree in the reticulum cells and histiocytes, especially in the reticulum cells of the liver.[2]

DESTRUCTION OF CHOLESTEROL

In spite of the ease with which the sterol ring system is synthesized, a disintegration of the cholesterol skeleton by enzymatic processes in the intermediary metabolism is apparently impossible. Negative-balance experiments were interpreted to indicate destruction of the sterol skeleton in the intermediary metabolism. Such a claim cannot be maintained, since bacteria of the intestines are able to convert cholesterol to products that are not precipitated with the customary reagents used in cholesterol determination. Bacterial disintegration of cholesterol in the intestines (but not in the intermediary metabolic processes) plays an important part in cholesterol metabolism.[3-8]

The changes that may occur on the cholesterol molecule‡ in the intermediary metabolism seem to be limited to the side chains such as esterification hydrogenation and oxidation. Furthermore, the metabolic changes occurring in the sterol hormones in the intermediary metabolism involve only their side chains.

ABSORPTION OF CHOLESTEROL

The absorption of cholesterol is facilitated by the presence of neutral fat in the intestines.[9] They are absorbed as cholesterol esters. Man absorbs only (or at least mainly) cholesterol of animal origin. Schoenheimer[10] demonstrated that sterols derived from plants are not absorbed in human beings. Herbivorous animals, however, absorb vegetable as well as animal cholesterol, but they are not able to excrete much animal cholesterol. The retained cholesterol in these animals is deposited within certain cells of reticular origin. For this reason herbivorous animals are not suitable for comparative studies of cholesterol metabolism.

EXCRETION OF CHOLESTEROL

Cholesterol is excreted with the bile as well as directly into the intestines.[11-13] The concentration

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‡Chaikoff and his co-workers (*J. Biol. Chem.* 194:413, 1952) described their experiments under the title "C^{14} Cholesterol. Oxidation of Carbon 4 and 26 to Carbon Dioxide by the Intact Rat." This title may lead to misunderstanding, since the authors report experiments that demonstrate that none of the ring carbon (C4 is ring A of the sterol molecule) was oxidized to CO_2. Only C26 of the Isoactyl side chain is oxidized to CO_2.

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of cholesterol in the bile fluid (liver bile)[14] is much lower than that in the serum. Cholesterol, as well as its bacterial-degradation products, is partly reabsorbed from the intestines. The reabsorption of bacterial-degradation products from the intestines may lead to a misinterpretation of experiments that are carried out for the purpose of proving a conversion of cholesterol into bile acids in the intermediary metabolism. Bloch and Rittenberg[15] injected deuterium-labeled cholesterol intravenously in dogs. The common bile duct of such a dog was anastomosed with the renal artery before the injection. Small amounts of deuterium-labeled bile acids were recovered in the urine of the animals. The result was considered a proof of the conversion of cholesterol into bile acids in the intermediary metabolism. However, one cannot exclude the possibility that in such an experiment deuterium-containing cholesterol was also directly excreted in the intestines and after bacterial disintegration reabsorbed as a deuterium-containing split product. The reabsorbed deuterium-containing material may have been used for the synthesis of bile acids in the liver. The bile acids, which have a different steric configuration from cholesterol, are synthesized in the liver independently of the cholesterol supplied by the blood, as our experiments have demonstrated.[16-19] The daily production of bile acids is as high as 2 to 3 gr., a figure that cannot be explained otherwise than by their synthesis in the liver independently from cholesterol supply by the blood stream. This cycle of excretion and reabsorption of cholesterol and its intestinal degradation products must be borne in mind in any consideration of sterol metabolism.

Function of Cholesterol

Despite the wide occurrence of cholesterol in the animal kingdom, its function in the organism remains unknown. It is thought that the correct mixture of the lipids present in every cell depends on an adequate amount of cholesterol and on its physical properties.

Another idea, though entirely hypothetical, should be mentioned. It is possible that the synthesis of cholesterol from acetic acid reveals another way in which the intermediary metabolism is able to dispose of an overload of acetic acid in case the Krebs citric-acid cycle is overburdened. Cholesterol formation would then be a device to prevent the accumulation of acetic acid in the organism and to transform it into a metabolically inert substance.

In an attempt to clarify the pathway of accumulation of cholesterol in the arterial tissue, the following points will be discussed:

The influence of the lipid compounds on the colloidal state of cholesterol in the serum; the conditions that lead to an *intracellular* accumulation of cholesterol in the superficial layer of the intact intima; and the conditions that produce an *extracellular precipitation* of cholesterol in the deeper layers of a primarily damaged arterial tissue.

It will be the purpose of this discussion to analyze whether two different pathways of cholesterol accumulation in the arterial wall are significant of a different pathogenesis of the arterial involvement in the hypercholesteremic group, on one hand, and the pathogenesis of the common type of arteriosclerosis of the older age group, on the other hand.

Lipid Constituents of the Serum that Influence the Colloidal State of Cholesterol in the Serum

Ratio of Total Cholesterol to Phospholipids

Cholesterol is hydrophobic in colloidal solution; lecithin, which constitutes about 80 per cent of the phospholipids in the serum, is hydrophilic. An increase of the hydrophilic phospholipids increases the stability of a colloidal solution containing both substances.[20, 21] The ratio of cholesterol to phospholipids in the serum is about 1, since the normal values for total cholesterol are 150 to 260 mg. per 100 cc. and for phospholipids 150 to 250 mg. per 100 cc. (calculated from 8 to 10 mg. per cent lipid phosphorus). It is evident that in cases of familial hypercholesteremia and in experimentally produced hypercholesteremia in rabbits, in which mainly cholesterol is increased in the serum, the cholesterol-phospholipid ratio is substantially higher than 1. In cases of primary and secondary hyperlipemia, however, in which both neutral fat and cholesterol and phospholipids are increased, the cholesterol-phospholipid ratio is usually normal. If one separates the cases of familial hypercholesteremia from the cases of arteriosclerosis of the higher age group (as always should be done), one finds that the cholesterol-phospholipid ratio in the arteriosclerotic group deviates so little from the normal range that it is questionable whether an increased cholesterol-phospholipid ratio alone should be responsible for the accumulation of cholesterol in the arterial wall. At this point the work of Kellner[22] should be mentioned. He fed or injected intravenously the detergents Tween 80 and Triton 20 in experiments with rabbits. Both detergents increased the stability of the colloidal state of the serum and lowered the cholesterol-phospholipid ratio. The application of detergents in human beings is not feasible because of disagreeable side-effects. Despite the doubtful value of the cholesterol-phospholipid ratio for diagnostic purposes, the fact remains that high phospholipid values in the serum and a consequent low cholesterol-phospholipid ratio favorably influence the stability of the colloidal state of cholesterol in the serum.

Cholesterol-Protein Aggregates; Lipoproteins

The colloidal solution of cholesterol and phospholipids is mainly influenced by various proteins.

Cholesterol and phospholipids associate with protein molecules of different sizes and different chemical structures. Indeed, the total amount of cholesterol and phospholipids in the serum is present in aggregates with various protein moieties, the so-called lipoproteins. The lipoproteins are not well defined chemical entities of uniform stoichiometric composition. They are present as perpetually changing protein aggregates with the apparent purpose of transporting cholesterols and phospholipids in the blood stream to and from the tissues and of maintaining their colloidal solution in the body. The standard methods of determination of lipids in serum and tissue do not account for the protein component of lipoproteins. The applied organic solvents in these methods precipitate the protein moieties and extract the protein-free lipids.

In the last decade much important work has been devoted to the characterization and purification of the various lipoprotein aggregates. It was thought that not so much the free lipids but certain fractions of lipoproteins and especially some more highly molecular types of lipoproteins may have some direct relation to the pathogenesis of arteriosclerosis.

Two different methods of characterization of lipoproteins were applied:

Cohn and his co-workers[23, 24] fractionated the lipoproteins from the serum according to their previous studies by electrophoresis. They designated as α-lipoproteins the lipoproteins isolated from α'-globulin fraction and as β-lipoproteins the lipoproteins from the β_1 globulin fraction. Alpha-lipoprotein contains about one third the amount of cholesterol present in the β-lipoprotein fraction, with slight variations of age and sex. Barr and his group[25, 26] used the Cohn methods of isolation of lipoproteins in pathologic cases. They demonstrated that in heterogenous hypercholesteremic conditions, such as familial hypercholesteremic xanthomatosis and hypercholesteremia in nephrosis, the α-lipoprotein fraction is decreased while the β-lipoprotein fraction is relatively and absolutely increased. In arteriosclerosis, however, an increase of the β-lipoproteins was either not marked or not found at all. It overlapped also with cases in which arteriosclerosis was not present but an increase of β-lipoproteins was found. Barr and his group[26] do not claim that an increase of β-lipoproteins in the serum is of diagnostic value for the presence of arteriosclerosis. However, they emphasize that in all conditions of hypercholesteremia, such as familial hypercholesteremia and nephrosis, the β-lipoproteins are increased and the α-lipoproteins are decreased. Consequently, the cholesterol-phospholipid ratio in these two fractions differed widely.

Gofman and his associates[27, 28] introduced a new method of investigation of lipoproteins, using the ultracentrifuge for this purpose. Large molecules of lower density than the solution in which they are present float at a certain boundary and at a certain speed in the ultracentrifuge. This floating layer of the centrifuged serum is pipetted out and again centrifuged in a constant solution of a lower density than 1.063. During the centrifugation of this solution the molecules move according to their molecular size. Their migration is recorded photographically by an optical system. The unit of migration by this method is called a "Svedberg unit." Various classes of lipoproteins, different in size, are registered in the serum. The largest molecule of 100 to 75 svedbergs include the chylomicrons. According to Gofman, these large molecules do not produce arteriosclerosis. In addition, the molecules of the 70- to 30-svedberg class, as well as the low-size class of less than 10 svedbergs, despite their high cholesterol content, should have no connection with the presence of arteriosclerosis. It is only the molecular species migrating at the rate of 10 to 20 svedbergs, of a molecular size of 3,000,000, that Gofman relates to arteriosclerosis.

Gofman and his associates[28] suggest that the larger molecules of the high-svedberg classes are progressively transformed into the lower-svedberg classes in the course of cholesterol and fat metabolism. He claims that the accumulation of 10- to 20-svedberg molecules is a metabolic error in lipid transport or a metabolic arrest at the 10- to 20-svedberg stage. Against the assumption that the S_{10} to S_{20} molecules are the result of a metabolic error of the lipid transport are the most recent experiments of Gofman and his group.[29] These investigators injected C_{14}- and P_{32}- labeled lipoproteins into cholesterol-fed rabbits. The serum of these rabbits contained, before injection, S_{10} to S_{20} molecules. Shortly after injection the labeled lipoproteins equilibrated uniformly with all svedberg classes of lipoproteins. The expected increase of labeled S_{10} to S_{20} molecules could not be demonstrated. In spite of the technical ingenuity of Gofman's experiments, the pathognomonic specificity of S_{10} to S_{20} molecules for the pathogenesis and diagnosis of arteriosclerosis still has to be proved, since S_{10} to S_{20} molecules, according to Gofman's figures, are also present in the serum of normal persons, though in smaller quantities, and they are not increased in all cases with coronary sclerosis and myocardial infarction. The question whether the determination and separation of lipoproteins or the demonstration of S_{10} to S_{20} molecules have diagnostic advantages in comparison with the customary determination of cholesterol and lipids is, in our opinion, not ripe for judgment. Keys[30] goes further in saying that "it is entirely unjustified to attribute to S_{10} to S_{20} molecules any special virtue beyond that for simple cholesterol measurements for the prediction of arteriosclerosis or the estimation of the activity of the arteriosclerotic process."

It should be emphasized at this point that any investigation of the relation of cholesterol to the pathogenesis of vascular changes is incomplete if this problem is approached only by an investigation

of the state of the lipid constituents in the plasma. It is obvious that both the physicochemical and the anatomic state of the structures of the arterial tissue in its reciprocal effect on the colloidal state of the plasma constituents is of equal if not superior importance. The pertinent problem of accumulation of cholesterol in the arterial wall cannot be solved by a one-sided investigation of the state of the serum lipids and their protein aggregates.

Accumulation of Cholesterol in the Arterial Wall

Intracellular Accumulation of Cholesterol

Our knowledge of the conditions that facilitate the normal exchange of plasma lipids through the intact arterial wall is inadequate.[31] The very fact that cholesterol may accumulate in the subintimal and intimal cells through the intact membrane of the intima is proof that a constant flow of cholesterol in colloidal solution passes through the structures of the intima into the lymph spaces of the arterial tissue.

A demonstrable accumulation of cholesterol in the intimal cells occurs only if the cholesterol content of the serum is considerably increased for a long period of time. Hypercholesteremia of long duration is, therefore, the pathogenic principle of this type of intracellular cholesterol accumulation. This type of cholesterol accumulation in the arterial intima (foam-cell formation, atheromatosis, xanthoma formation) is characteristic of familial hypercholesteremia*[32-35] and of experimentally produced hypercholesteremia in animals.[36-40] The initial lesion in both instances is the same, namely, large layers of cushions of cholesterol-loaded cells in the intimal and subintimal layer (Fig. 1). The clusters of these cells of foamy structure may bulge the intact surface of the intima. The single lesion is limited to a circumscribed area. The arterial system is not involved in its entirety. The lesion may recede completely (milk streaks in infants and children), and fibrosis may not develop if hypercholesteremia does not persist for a long period. However, if the cholesterol feeding in rabbits is continued for a long time some lesions disintegrate and fibrotic tissue develops into the softened lesion. At this stage of experimental hypercholesteremia fibrosis also penetrates into the deeper layers, causing sclerosis of the arterial wall. Extracellular precipitation of cholesterol in this late phase may occur secondarily to the sclerosing process.

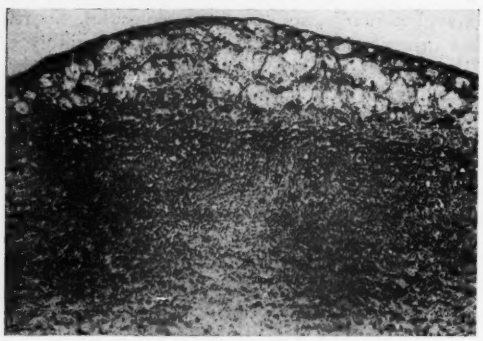

FIGURE 1. *Example of Intracellular Accumulation of Cholesterol and Its Esters: Xanthomatous (Atheromatous) Nodules of the Intima of an Artery (Courtesy of Dr. Timothy Leary). Reproduced from Thannhauser.*[33]

Familial hypercholesteremia. There is, however, a certain variance between experimental hypercholesteremia in animals and the human conditions of hypercholesteremia. The load of cholesterol in experimental hypercholesteremia in rabbits is much greater than in any condition of human hypercholesteremia, since human beings are able to excrete cholesterol whereas the herbivorous animals have no means of excreting massive doses of fed or injected cholesterol. It is, therefore, understandable that the intracellular accumulation of cholesterol in the subintimal layer does not disintegrate in human familial hypercholesteremia as rapidly as in experimental hypercholesteremia in animals. In fact, the subintimal clusters of foam cells in human hypercholesteremia may persist for a lifetime without softening and disintegration. Consequently, fibrosis of the vessel wall in cases of human hypercholesteremia may not develop at all or may be present only in a small localized area of the vascular tree. The consequences, however, may be catastrophic if the lesion is located in the coronary vessels. We do not know why the coronary vessels are so often the site of such a lesion in familial hypercholesteremia. It should be kept in mind that in both human and animal hypercholesteremia the accumulation of cholesterol in the serum is the primary cause and the pathogenetic agent of the intimal lesion.

Patients of the familial-hypercholesteremia group were included in the clinical studies of the common type of arteriosclerosis. Thus, the impression was created that high serum-cholesterol values occur in the common type of arteriosclerosis and are of pathogenetic importance in this condition. This error is understandable, as familial hypercholesteremia is not so rare a hereditary anomaly of cholesterol metabolism as we formerly believed. Familial hypercholesteremia, originally described by Thannhauser and Magendantz[32] as the forme fruste of familial hypercholesteremic xanthomatosis, however, must be distinguished from the common type of arteriosclerosis of the higher-age group.[33, 34]

*Hypercholesteremia in idiopathic hyperlipemia and in conditions of secondary hyperlipemia (lipid nephrosis and diabetes) must be distinguished from familial hypercholesteremia in respect to its etiology and its clinical significance. In idiopathic hyperlipemia and lipid nephrosis the cholesterols and phospholipids (and in particular the neutral fats) are elevated, whereas in familial hypercholesteremia (forme fruste of familial hypercholesteremic xanthomatosis) neither neutral fat nor phospholipids are notably increased in the serum. Vascular involvement, in contrast to diabetes, is rarely observed in idiopathic hyperlipemia or lipid nephrosis.

The diagnosis of familial hypercholesteremia should be accepted only if the serum cholesterol of several members of the same family has been found to be increased.[41] If we eliminate patients of the familial hypercholesteremic group in a study of the pathogenesis of the common type of arteriosclerosis, the serum-cholesterol values in patients with generalized arteriosclerosis are usually in the normal range and in a fasting state rarely exceed 300 mg. per 100 cc. The accumulation of cholesterol in the arterial wall, as present in the common type of arteriosclerosis, cannot, therefore, be explained by a primary accumulation of cholesterol in the serum. What, then, is the process that causes the accumulation of cholesterol in arterial tissue in the common type of arteriosclerosis despite normal serum cholesterol?

Extracellular Cholesterol Precipitation in the Common Type of Arteriosclerosis

It has already been mentioned that cholesterol circulates in the blood stream as a colloidal solution aggregated with various protein moieties. The colloidal state of the cholesterol solution in the plasma is maintained while it circulates through an intact arterial tissue. If, however, the colloidal solution of cholesterol passes through a damaged arterial tissue[33, 34] and comes in contact with the altered tissue colloids and with the fibrosed anatomic structures, the colloidal state of the transuding cholesterol solution breaks down, and cholesterol precipitates or crystallizes *extracellularly* in the widened tissue spaces (Fig. 2). Extracellular cholesterol precipitation and crystallization are not dependent on the cholesterol concentration of the plasma and take place in cases with normal concentration of cholesterol in the serum. Cholesterol accumulation by precipitation of cholesterol in the damaged arterial tissue is then secondary to primary changes of the arterial structures. For this reason extracellular precipitation may be considered a predominant pathway of cholesterol accumulation in the altered arteries of the common type of arteriosclerosis. Histologic examination in advanced phases of arteriosclerosis shows, in addition to the masses of cholesterol precipitated, scattered lipid-loaded cells in the deeper layers of the arterial tissue. The development of foam cells in the deeper layers of arteriosclerotic tissue is different from that seen in the initial lesion in the intimal layer of familial and experimental hypercholesteremia. In the latter cases the intracellular accumulation of cholesterol in the intimal cells originates from a cholesterol uptake directly from the circulating blood, while the phagocytic cells present in the deeper layers of an arteriosclerotic vessel accumulate lipid detritus from the cholesterol primarily precipitated in the tissue spaces. The presence of cholesterol in the form of an amorphous or crystallized precipitate in the sclerosed arterial tissue often may not be recognized on gross inspection. Histologic examination with fat stains, — or, better, with quantitative determination of cholesterol in the sclerosed tissue,[42] — is necessary to reveal the extracellular type of cholesterol accumulation in the arterial tissue.

Calcium deposition. Not infrequently, calcium is deposited, together with cholesterol, in the arteriosclerotic tissue, because calcium is also present up to 50 per cent as colloidal calcium-protein aggregate in the plasma. It is, therefore, not astonishing that a derangement of the colloidal state of the plasma by the damaged arterial tissue leads to a precipitation of cholesterol as well as of calcium.[43] However, no one would claim that the precipitation of calcium in the arterial wall is a primary disturbance of calcium metabolism or that the calcium-protein aggregate of itself would cause arteriosclerosis, as is claimed for cholesterol.

It is possible that the colloidal properties of the cholesterol and calcium-protein aggregates in the serum, — that is, their molecular size and the configuration of the protein moieties, — directly influence their precipitation. It is more likely, however, that the *reciprocal* effect of the altered tissue colloids on the various plasma colloids results in the breaking down of their colloidal state and in their extracellular precipitation and accumulation in an altered arterial tissue. There is not enough evidence, as yet, that a specific protein-cholesterol aggregate such as a lipoprotein of the S_{10} to S_{20} class is the single provoking factor of so complex a process as the pathogenesis of the common type of arteriosclerosis.

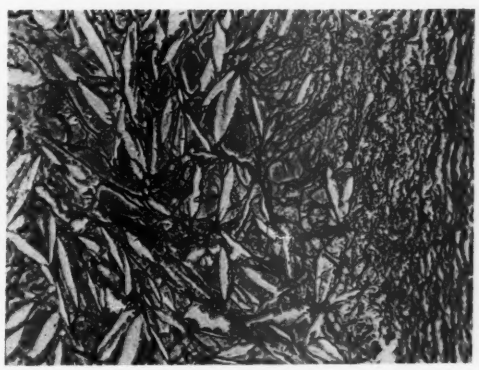

FIGURE 2. *Example of Extracellular Precipitation and Crystallization of Cholesterol: Atheroma of Human Aorta (Reproduced from Altschul,[38] by Permission of the Publishers).*

I have attempted to show that cholesterol accumulation in the arterial wall may follow two different pathways.

One pathway is the intracellular accumulation of cholesterol as manifested in familial hypercholes-

teremia and experimental hypercholesteremia in animals. In these conditions the intracellular accumulation of cholesterol in the intimal and subintimal cells takes place without primary damage of the arterial tissue but is the result of cholesterol accumulation in the circulating blood stream.

The second pathway is the extracellular cholesterol precipitation and crystallization as seen in the common type of arteriosclerosis. The process of cholesterol precipitation in the damaged arterial wall proceeds irrespective of cholesterol content of the serum but is secondarily provoked by a primary alteration of the arterial tissue. Both processes of cholesterol accumulation in the arterial tissue overlap in advanced stages of disease.

Pathogenesis of the Common Type of Arteriosclerosis

What, then, is the pathogenesis of the primary alteration of the arterial tissue in the common type of arteriosclerosis in the higher-age group? Various and different pathogenetic factors may lead to a primary alteration of the arterial tissue that is consequently, later in life, followed by generalized or localized arteriosclerosis. As far as one can judge, there is no uniform pathogenetic principle that causes the common type of arteriosclerosis.[38, 44-49]

It is assumed that a "wear-and-tear" process involving especially the elastic structures of the arterial wall is the primary cause of arteriosclerosis. A more modern expression of this conception attributes the changes resulting from "wear and tear" to the aging of the colloids of the elastic fibers and their elastic ground substance. The changes of the colloidal stage of these structures are thought to be responsible for the precipitation of the circulating colloidal solution of cholesterol and thus to cause the accumulation of cholesterol in the arterial wall.

It has been demonstrated (Winternitz,[46] Schlichter[50] and others[51]) that deterioration of the vasa vasorum may result in changes of the tissue of larger arteries that lead to arteriosclerosis and to secondary precipitation of cholesterol.

Inflammatory processes of heterogeneous origin,[47] — for example, syphilis, especially in localized areas of the arterial system, — may be followed by precipitation of cholesterol in the affected parts.

A disturbance of the enzymatic process of the arterial tissue vital for cell respiration and necessary for the disintegration of energy-supplying metabolites may result in alteration of the arteries. An example of such a process is, in my opinion, the tendency to arterial damage in diabetic patients. The concept that the high fat and cholesterol content of the plasma of diabetic patients alone is the primary cause of the frequency of arteriosclerosis in diabetics does not agree with the clinical experience. Juvenile diabetic patients may develop severe vascular changes without considerable increase of lipids in the plasma. On the other hand, progressive arteriosclerotic manifestations may be observed in adult diabetic persons despite the fact that the fat and cholesterol content of the plasma is kept within normal range by restriction of fat in the diet and by insulin. For these reasons it seems likely that the alteration of the arteries of diabetic patients is primarily caused by a disturbance of an enzymatic process related to the basic disturbance of carbohydrate disintegration rather than to an accumulation of cholesterol and fat in the serum. The precipitation of lipids in the altered arterial wall of a diabetic patient proceeds secondarily if the cholesterol and fat content of the serum increases after a period of uncontrolled diet.

Dietary Treatment

The demonstration of two different pathways of cholesterol accumulation in the arterial tissue is not only of value for an explanation of the pathogenesis of the arterial involvement in the hypercholesteremic group, on one hand, and the arteriosclerotic group, on the other hand, but is also of importance to therapy in these conditions.

In familial hypercholesteremia, the problem is to reduce the cholesterol content of the serum; in the arteriosclerotic group, a reduction of the cholesterol content of the serum is of questionable importance, since the precipitation of cholesterol in a damaged arterial wall is independent of the cholesterol level in the serum. The task of reducing an increased cholesterol content of the body fluids to normal values is difficult if not impossible. Such an attempt is often unsuccessful, as cholesterol is constantly synthesized in the body and there is no means of influencing the synthetic process. The problem may be approached in the following ways:

By elimination of cholesterol-containing foodstuffs from the daily menu; eggs, butter, cream and meat are the foodstuffs of the highest cholesterol content.

By restriction of the intake of fat, since the presence in the intestines of any kind of neutral fat, of either animal or vegetable origin, increases the absorption of cholesterol[52]; unfortunately, one cannot restrict neutral fat entirely from the diet. Food with no fat becomes unpalatable. A diet of around 1700 calories, containing 20 to 30 gm. of fat (mainly in the form of pure vegetable fat), 80 gm. of protein and 300 gm. of carbohydrates, seems appropriate in familial hypercholesteremia.

By administration of 1 to 2 gr. of thyroid daily; thyroid should not be prescribed for a patient complaining of anginal pain.

By the use of choleretic substances one could theoretically increase the excretion of cholesterol in the bile; however, the choleretics presently at our disposal, such as bile acids, are not efficient enough for this purpose.

The use of so-called lipotropic substances like cholin, methionin or inositol was not effective in our hands in reducing the serum cholesterol.

The intravenous injection of 20 to 100 mg. of heparin was recently recommended by Gofman and his associates[53] for arteriosclerosis. Hahn[54] originally discovered that the injection of 3 mg. of heparin after a fat meal changes the milky appearance of neutral fat in the serum to a more transparent solution. Apparently heparin has an effect on the colloidal dispersion of neutral fat and lipoproteins in the serum. We have no knowledge of whether or not heparin has any influence on the amount of cholesterol circulating in the blood.[55]

A diet low in cholesterol and neutral fats is recommended in familial hypercholesteremia as well as in conditions associated with hyperlipemia. However, in the treatment of the common type of arteriosclerosis of the higher-age group, the restriction of cholesterol will not have the desired effect on the progression of the sclerotic changes of the arteries. In these cases, a diet low in calories (50 gm. of neutral fat), irrespective of its content of cholesterol-bearing foodstuffs, seems to be sufficient.

Summary

The mechanism of cholesterol accumulation in the arterial tissue cannot be explained by a one-sided investigation of the physical properties of the lipid constituents and their protein aggregates (lipoproteins) in the plasma. The anatomic and physical properties of the arterial tissue are of equal importance in the accumulation of cholesterol in this tissue.

Two processes of cholesterol accumulation in the arterial tissue should be distinguished: *intracellular accumulation of cholesterol in the intimal and subintimal cells*, in which the accumulation of cholesterol in the serum is the primary cause of the arterial lesion, and *extracellular precipitation and crystallization of cholesterol in a primarily altered arterial tissue*, in which extracellular precipitation of cholesterol occurs independently of the cholesterol level of the serum. Calcium deposition and cholesterol precipitation in the altered arterial wall are probably analogous physicochemical processes secondary to the structural and physical changes of the tissue.

Familial hypercholesteremia, being the forme fruste of familial hypercholesteremic xanthomatosis, should be pathogenetically and clinically distinguished from the common type of arteriosclerosis of the higher-age group.

Different dietetic regimens are suggested for patients with familial hypercholesteremia and patients suffering from the common type of arteriosclerosis of the higher age group.

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MEDICAL INTELLIGENCE

ACUTE INTESTINAL OBSTRUCTION CAUSED BY MACARONI*

Report of a Case

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PROVIDENCE, RHODE ISLAND

A REVIEW of the literature reveals that intestinal obstruction by food substances is not uncommon. In 1932 Elliot[1] collected 40 cases caused by mushrooms, cherry stones, beans, figs, oats, potatoes, apples, pears, peas, corn, grapes, poppy seeds, "ammunition bread," sauerkraut, gooseberries, raisins, oranges, popcorn and bran. In 1939 DeBakey and Ochsner[2] collected 126 cases of phytobezoars of which 73 per cent were composed of persimmons. Phytobezoars were found to occur three times more commonly in males than in females. We have been able to find 42 cases[3-20] of small-bowel phytobezoars reported since 1940. These were composed of apricots, oranges, carrots, persimmons, bran, apples, peaches, currants, wheat, almond, watercress, prune pit and lettuce. Other substances that have been reported include prunes, plums, celery, cocoanut fibers, tobacco, dates, watermelon, peanuts, butter beans and sweet potatoes. Apparently, any food capable of increase in size by imbibition of fluid, especially if it contains a large proportion of indigestible material such as cellulose, can become a bezoar. Abnormalities such as poor dentition, gastroenterostomy, intestinal stricture and intraperitoneal adhesions may be contributing factors in the production of intestinal obstruction due to bezoars.

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Case Report

F. L. (No. 7885), a 37-year-old man, was admitted to the Veterans Administration Hospital for the second time on September 29, 1951. His first admission was in June, 1950, when a postcolic Hofmeister-type subtotal gastrectomy was performed for intractable gastric and duodenal ulcers. The postoperative course had been uneventful. The patient remained well after discharge from the hospital until the day before his second admission, when he suddenly experienced severe generalized, crampy, nonradiating abdominal pain accompanied by vomiting. His bowel movements had been regular. He had no other complaints referable to the gastrointestinal tract.

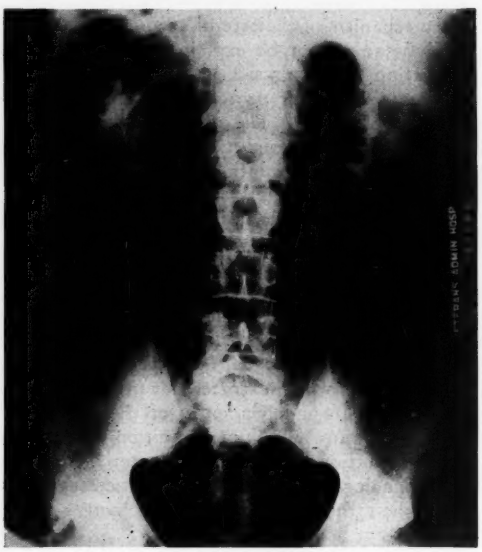

Figure 1. *Flat Film of Abdomen the Day After Admission.*

On physical examination the temperature was 97.6°F., the pulse 72, the respirations 20 and the blood pressure 144/90. The patient appeared acutely ill and experienced intermittent doubling-up abdominal pain. Episodes of pain were accompanied by gurgling sounds that could be heard several feet away. The abdomen was moderately distended and auscultation revealed peristaltic rushes. Between attacks of pain the abdomen was completely quiet. Slight deep tenderness was present in the epigastrium. There was no rebound tenderness or spasm. A well healed left upper paramedian scar

was noted. The remainder of the examination revealed no abnormality.

Laboratory examination revealed a hemoglobin of 14.5 gm. On admission the white-cell count was 14,000, with 86 per cent polymorphonuclear leukocytes (7 per cent nonsegmented) and 14 per cent lymphocytes. Immediately prior to operation the white-cell count was 8500 with 76 per cent polymorphonuclear leukocytes (6 per cent nonsegmented), 24 per cent lymphocytes and 1 per cent monocytes. The serum chloride was 95 milliequiv. per liter, the serum carbon dioxide 22 milliequiv. per liter and the blood urea nitrogen 13 mg. per 100 cc. Flat and upright roentgenograms of

FIGURE 2. *Bolus Composed Largely of Ingested Macaroni.*

the abdomen revealed dilated loops of small bowel, presumably jejunum, with fluid levels. On the following day repeat roentgenograms revealed a slight increase in the number of dilated loops of bowel (Fig. 1).

After admission the patient continued to vomit, until a Harris tube was passed into the stomach and connected to suction. The cramps diminished somewhat in intensity but did not disappear. The patient was given intravenously fluids containing glucose, sodium chloride and potassium chloride. The latter was added only after the patient had been well hydrated. On the morning following admission the patient was subjectively unimproved. Tenderness in the epigastrium was slightly more severe. Distention was slightly more marked. The rectal temperature and pulse had risen to 101.2 and 92 respectively. The Harris tube had not entered the jejunum. On the day after admission laparotomy was performed; an obstruction was located in the ileum. The proximal loops of bowel were markedly dilated; the distal loops were collapsed. At the point of obstruction a firm intraluminal mass was identified. The mass could not be moved or broken up without risking injury to the bowel. Accordingly, an enterotomy was performed and a bolus of what was later identified as macaroni was removed (Fig. 2). Postoperatively, the patient recovered without complications. The patient later stated that he had eaten macaroni four days prior to admission.

An important predisposing factor in this patient's difficulties was the presence of a gastroenterostomy. There were 4 instances of gastroenterostomy in the 42 cases collected from the literature.

SUMMARY

Obstruction of the small intestine due to food substances is not uncommon.

A case of intestinal obstruction due to macaroni is reported.

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MANHATTAN

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38181

PRESENTATION OF CASE

A fifty-six-year-old man was admitted to the hospital because of progressive loss of power in his legs.

Four months prior to entry, the patient for one month noted intermittent dull pain over the lateral aspect of the left calf that was not in any way incapacitating. Three months prior to admission on awakening one morning he noted stiffness and pain in the left ankle, knee and hip. He worked that day, but by the next morning the pain and stiffness were so severe that he was unable to get out of bed. He remained at home for one week; since walking seemed to ease the difficulty he did as much of this as possible and seemed to improve considerably over the next week, but the pain and stiffness returned. Next he developed numbness in the left foot that subsequently spread to involve the whole leg. The symptoms were less severe when he was off his feet; for this reason he remained in bed for three weeks. At the end of this time, despite the persistence of the symptoms, he decided he would "try and walk off the symptoms"; he was able to walk with crutches but continued to have severe pain in the left ankle and leg. Two weeks before admission, numbness in the right foot appeared and was followed shortly thereafter by stiffness and pain in the right leg; by this time he was able to get relief from the pain only by lying on his back. Shortly after the onset of the right-leg pain he was admitted to another hospital, where he remained for one week; roentgenograms of the chest, lumbar spine, pelvis and knees were negative, and the spinal fluid was found to contain 46 mg. of protein and 120 mg. of sugar per 100 cc. One week before admission he noted that he was not able to ascertain when he started or stopped the urinary stream, although he was still conscious of the desire to urinate. Four days prior to entry he was unable to urinate and since then had to be catheterized. Shortly thereafter he began to lose bowel control and would lose small amounts of feces when he stood up. He continued to be able to move his legs fully, although they were weaker than normal. He had lost about 30 pounds in weight. There were no other symptoms.

Physical examination revealed a well developed man who found it difficult to change his position in bed. Except for a completely relaxed rectal sphincter, all abnormal physical findings were limited to the lower extremities. There was mild but definite weakness of the legs and feet; the examination was made difficult by pain in the knees that seemed to hinder movement more than did true weakness. The glutei and calf muscles were atrophied. The knee jerks were normally active and equal; the left ankle jerk was absent and the right ankle jerk barely obtainable. Sensation to pinprick and light touch was impaired in the sole and lateral aspects of the right foot and ankle and over both buttocks, with subjective numbness (but no objective sensory change) in the left foot. Vibration and position sense were normal. There was no tenderness on palpation of the lower back or sacrum.

The temperature was 98°F., the pulse 76 and the respirations 18. The blood pressure was 140 systolic, 80 diastolic.

Examination of the blood showed a hemoglobin of 14.4 gm. and a white-cell count of 13,100, with 78 per cent neutrophils. A urine of specific gravity 1.028 was negative. The spinal fluid contained 6 red cells and 3 white cells per high-power field and 138 mg. per 100 cc. of protein. A myelogram showed complete arrest above the level of the fourth lumbar disk. Roentgenograms of the lumbosacral vertebras showed straightening of the normal curvature, minimal lipping above the margins of the lumbar vertebral bodies and slight generalized demineralization of the bones. X-ray films of the lower dorsal and upper lumbar spine were negative.

There was no change in his condition while in the hospital; on the ninth day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM H. SWEET*: "He remained at home for one week; . . . seemed to improve considerably over the next week, but then the pain and stiffness returned." It looks as though there was at least a partial remission.

"Two weeks before entry numbness in the right foot appeared . . . ." The trouble spread to the other side only shortly before admission.

"The spinal fluid contained . . . . 138 mg. per 100 cc. of protein." The elevation of the total protein in the spinal fluid was marked, whereas it had been 46 mg. a few weeks before.

Would you show the x-ray films? As a matter of fact, it seems that the only clue I am able to obtain

*Associate visiting neurosurgeon, Massachusetts General Hospital.

is likely to arise from a careful appraisal of the appearance of the myelogram.

DR. JOSEPH HANELIN: The films of the lumbar spine were not interpreted as showing any definite bony changes, although one might wonder about some increased rarefaction of the fifth lumbar vertebral body in the myelogram.

DR. SWEET: That is not particularly exciting. The fourth and fifth lumbar vertebras had a small questionable shadow in them. How much weight would you place on that?

DR. HANELIN: The original interpretation made no mention of bone involvement. The myelogram shows a complete block opposite the fourth lumbar interspace that is fairly typical of an extradural type of lesion.

DR. SWEET: The contrast medium was put in from above, so the blocking is approximately at the junction of the fourth-fifth lumbar interspace.

DR. HANELIN: That is correct; it is almost directly over the interspace.

DR. SWEET: Especially in the oblique view.

Without reviewing the symptoms and signs that have been so clearly set forth here, I think it suffices to say that all of them are readily explainable on the basis of a space-taking mass in the lowest part of the lumbar spinal canal and that I need not seek some other portion of the body to account for the pain or other sensory disturbances, the weakness, the disturbances of bowel and bladder, the atrophy in the leg muscles and the gross diminution in ankle jerks, although the knee jerks were present. All these fit in with the lower motor neuron type of lesion that I should anticipate from a space-taking lesion in the lower part of the cauda-equina region. The differential diagnosis, therefore, is that of a space-taking mass.

In this age group, especially when symptoms moved along at this rate in a man who had lost 30 pounds in weight, I must certainly seriously consider the possibility of some form of malignant disease. Very commonly we find that the first evidence of a malignant tumor arising somewhere else is a lesion in the spinal canal metastatic from a primary source. In males, probably the commonest source of these malignant tumors is the prostate; that may be the source even though no abnormal nodule is palpable in the prostate on rectal examination, as was the case here. In women, of course, lesions arising from the breast or from the uterus are also frequently metastatic to the spinal canal.

Among the other malignant tumors are sarcomas, which we commonly see in this region, arising from the connective tissue — not eroding the bone in any fashion that is demonstrable in the radiologic examination but nevertheless causing the first symptoms in this manner. Another primary type of tumor in this region is multiple myeloma, with which there is commonly evidence of erosion of the bone, especially of the vertebral bodies. Apparently multiple myeloma was not considered too seriously, as no studies were made for Bence–Jones protein in the urine or of the total protein in the serum.

Other less common types of space-taking lesions or lesions that will produce an arrest of Pantopaque in the spinal canal include chronic arachnoiditis, which we have been seeing lately. Formerly, I think, we used to see this only on a totally unexplained idiopathic basis, but more recently we have seen a number of cases of chronic arachnoiditis that developed in patients who had had spinal anesthesia, in patients who had frank infections in the region and in patients who apparently had trauma subsequent to operations even though the dura had not been opened. There were no such antecedent episodes in the history in this case to suggest that type of disorder. When we do see chronic arachnoiditis, we do not often see in the roentgenograms quite as sharp a cutoff of the flow of the contrast medium as is seen here; usually there is some irregularity of the shadow, although we have seen one case in which it was sharply cut off, suggesting a space-taking lesion or some other solid blocking mass.

There are a number of other types of extradural lesion that one may see. An extradural cyst may develop as a consequence of the outpouching of the arachnoid along the root sheath. This may present outside the dura at the cauda equina as a space-taking mass, because spinal fluid becomes trapped in the pouch.

Another type of lesion that is exceedingly unusual in this locality is an echinococcus cyst in the spinal canal. The only case I have ever seen was one I saw in England.

I have not yet mentioned the intradural lesions in the cauda equina. The commonest of these are neurofibromas and meningiomas. Meningiomas usually develop over a longer period of time than the four months shown in this history. Moreover, I would think it rather unusual for a meningioma or neurofibroma to cause so abrupt an increase in the total protein in the spinal fluid as appeared to take place in this patient. I would have anticipated that both the first and second lumbar punctures would have shown a high total protein if there were an intramedullary lesion causing this. It seems more likely that an extradural lesion that had perhaps abruptly grown large enough to close off the lowermost end of the spinal canal would cause this apparent abrupt increase in total protein than would an intramedullary space-taking lesion — that is to say, one inside the spinal cord arising in the conus and spreading on down here; of course, there is no spinal cord in this level under ordinary circumstances.

For these reasons I move back to a consideration of extradural space-taking lesions in this region. Of course, by far the most common is a protrusion of the intervertebral disk in this interspace or the in-

terspace below. The fact that this lesion was large enough to cause a complete block and yet lay athwart the interspace, in the upper half of the interspace, does not necessarily rule out a massive protrusion of the disk, as we have often seen them roll over the posterior surface of the centrum of the vertebra above and below so that the main part of the lesion actually lay opposite the vertebral centrum rather than opposite the disk interspace. One feature of the films that argues against a massive protrusion of the intervertebral disk is that the interspace between the fourth and fifth lumbar vertebras is not narrowed. However, on a statistical basis, the facts that this is by far the commonest lesion occurring in the fourth to fifth interspace and that there was one period of at least moderate easement, although not actually complete regression of the symptoms, which is characteristic of the behavior of a protruded intervertebral disk, incline me to make as my first choice an intervertebral disk protrusion. I shall also mention one more point — that many of the cases with metastatic tumors have a much more rapid history than the four-month period in this case, although a substantial number of them run along for quite a while.

Dr. Walter Bauer: Was there any febrile course?

Dr. Sweet: Only one temperature was recorded; that was normal.

Clinical Diagnosis

Ruptured intervertebral disk.

Dr. Sweet's Diagnosis

Ruptured intervertebral disk.

Anatomical Diagnosis

Plasma cell myeloma.

Pathological Discussion

Dr. Benjamin Castleman: Dr. Charles S. Kubik, who saw the patient before he made the myelogram, observed some of the outside films and thought that the fifth lumbar vertebra was somewhat abnormal. When the films were repeated here, he agreed that the vertebra was not abnormal, and after the myelogram he believed that the condition was consistent with a ruptured disk, although he did say that the severe persistent pain raised the question of metastatic tumor. Dr. Joseph Barr, who also saw him, agreed that this probably was a ruptured disk. Would you tell us about the operation, Dr. Ballantine?

Dr. H. Thomas Ballantine: At operation we began our exploration from the left side, because the symptoms were predominantly left-sided. We did a hemilaminectomy in an attempt to expose the extradural mass. It was impossible to do so because the mass lay absolutely centrally placed anterior to the dura. Consequently, we did a complete laminectomy at the fourth lumbar to fifth lumbar vertebra. Protruding upward into the spinal canal was a mass about 1.5 cm. in diameter, which also protruded inward about a centimeter and was bluish; on incising the dura we came down on very friable reddish tumor tissue that extended through the interspace, down into the body of the fifth lumbar vertebra and possibly upward into the body of the fourth lumbar vertebra. We did as radical a removal as we could but thought that we had left tumor behind. After the excision, because we thought closure of the dura would cause pressure on the nerve roots of the cauda equina in the tumor area, we left the dura open. Subsequently the patient did quite well and was able to be up and around, with increased strength in flexors and extensors of the feet, but still had difficulty with his bladder.

Dr. Castleman: On frozen section this was called a plasma-cell myeloma, and this diagnosis was confirmed on permanent sections. Following this diagnosis other studies were done, which did not show further evidence of myeloma; that is, the serum protein was normal and there was no urinary Bence–Jones protein. An aspiration of the marrow did show 8 per cent plasmacytes, which Dr. Bernard M. Jacobson says is consistent with a slowly growing multiple myeloma.

Dr. Hanelin: A film of the shoulder shows several cystic areas in the scapula that could be due to myeloma. After the laminectomy, additional films of the spine were made that showed the vertebras to better advantage; there is definite evidence of involvement of the fourth and fifth lumbar bodies. I think, in retrospect, going over the original films, that there was evidence of involvement of the fifth lumbar vertebral body.

CASE 38182

Presentation of Case

A sixty-two-year-old woman was admitted to the hospital because of a mass in the neck.

Seven weeks before entry the patient first became aware of a small lump in the right side of the neck. Three weeks before admission, the physician who examined her described a 2-cm. hard lump in the region of the right thyroid lobe. The isthmus of the thyroid and the left lobe were palpable but not abnormal. One week prior to admission the patient complained, for the first time, of tightness in the left side of the neck. Examination of the neck disclosed no change in the mass in the right thyroid lobe, but the isthmus was more palpable and a hard diffuse enlargement of the left lobe was noted. There was no demonstrable cervical lymphadenopathy. During several nights of the week before admission she had several chills, but she had not been aware of any definite fever.

Her general health had been excellent. She had had arthritis in both knees for four years but had been relieved of all symptoms following one month's therapy with cortisone ten months prior to entry.

Physical examination revealed a well nourished woman in no distress. There was a firm, nontender, freely movable mass in each of the lobes of the thyroid. The heart, lungs, abdomen and extremities were normal.

The temperature was 98.6°F., the pulse 100 and the respirations 20. The blood pressure was 140 systolic, 80 diastolic.

The urine, of specific gravity 1.005, was normal. The twenty-four-hour uptake of a tracer dose of I^{131} (radioactive iodine) by the thyroid gland was 6.1 per cent; there was no unusual localization of function.

On the third day an operation was performed.

Differential Diagnosis

Dr. William V. McDermott, Jr.*: This case presents me with a simplicity of detail; briefly, this woman of 62, with the exception of the arthritis, had been in good health until the onset of the illness seven weeks prior to admission. The illness consisted of an asymptomatic lump in the neck that three weeks before admission was found by a physician to be in the right lobe of the thyroid gland; the remainder of the thyroid was normal. In the ensuing two weeks, the process apparently spread rapidly to involve the isthmus and left lobe as well. The other point in the history and in the hospital workup at that time was that the patient had a few chills during the week prior to entry without evidence of systemic infection or systemic manifestations of disease. The only pertinent laboratory finding was the radioactive-iodine uptake of 6.1 per cent, which indicates an almost complete suppression of thyroid function. Aside from that and the diffusely enlarged, firm, nontender thyroid gland noted on physical examination, there was nothing remarkable.

In the differential diagnosis, I think I can reasonably and quickly eliminate certain possibilities. A nontoxic nodular goiter is out of the question because of the rapid onset of the disease and the low function of the thyroid; that would not be expected in the usual nontoxic nodular goiter. There was no evidence of toxicity, so I can rule out hyperplasia on that basis, if not on the basis of rapidity of progression of symptoms. That leaves me with the possibilities of neoplasia or inflammation. Papillary adenocarcinoma or alveolar-cell carcinoma of the thyroid would most certainly not present this picture of a rapidly spreading, diffuse process in the thyroid over this short period of time. Carcinoma simplex or round-cell carcinoma is a wildly growing tumor at onset but does not usually have this short a history of spread. I can be supported in ruling out this possibility by the fact that carcinomas traditionally do not suppress thyroid function to this degree because they do not diffusely involve all thyroid tissue; it is extremely unusual in malignant disease of the thyroid to have almost complete absence of function despite a widespread involvement by neoplasia. That leaves me with the differential diagnosis among thyroiditides.

Can I be more specific in the diagnosis than to use the vague generic term of thyroiditis? There is enough information to break down this broad generalization. As I consider the various types of thyroiditides, I think it would be fair to rule out the very rare specific types, such as those due to syphilis or tuberculosis and the suppurative types due to bacterial invasion. There was nothing in the picture to suggest any of these diseases.

The nonspecific group of thyroiditides may be subdivided still further into the acute, subacute and chronic types. Acute thyroiditis certainly would not be expected to follow this pattern. I should expect more systemic manifestations and more local signs around the thyroid, such as pain, tenderness or an actually inflamed thyroid gland. That leaves me with the subacute and chronic types.

In the group of inflammatory diseases of the thyroid, which we classify as chronic thyroiditis, are two main categories, Riedel's struma and the struma lymphomatosa of Hashimoto. Classically the pathologic process of Riedel's struma is one of a slow and insidious onset, with the history extending back a number of years and, surprisingly enough, despite the hard fixed thyroid that is found on physical examination, with only rarely extreme suppression of the thyroid function. I think it would be fair enough on the physical examination, the history and the minimal laboratory data available to rule out Riedel's struma.

Hashimoto's struma is more appealing in many ways. First of all, it appears in women in or around the menopause, in which category this woman falls. The description of the gland on physical examination fits the typical pathologic picture presented by Hashimoto's disease, in that the mass was painless and nontender and showed minimal symptoms on slight pressure in the neck. The end stage of Hashimoto's disease is frequently one of myxedema with complete suppression of thyroid function; the radioactive-iodine uptake of 6.1 per cent in this patient tends to support that diagnosis. On the other hand, one point that is somewhat against consideration of Hashimoto's disease as a final diagnosis is the type of onset in this case. In the several series of cases of Hashimoto's disease reported in the literature, the average duration of symptoms ranged from fifteen months to over two years. Nevertheless, this fact alone does not completely rule out this possibility, as there are a few reported cases with a much more rapid progress, and I think all of us have seen at least one case of Hashimoto's disease, even though it is rare, in which the symptoms lasted a

*Assistant in surgery, Massachusetts General Hospital.

matter of weeks rather than months or years. This certainly cannot be ruled out, although the course presented by this patient would be quite atypical.

I have saved to the end the consideration of the entity of subacute thyroiditis, which was first described by DeQuervain[1] in 1936. This is a rare entity, even among the rare group of thyroiditis cases. Nevertheless there is much in this case that would tend to support this diagnosis. First of all, this disease typically has a rather rapid onset that begins in one lobe of the thyroid and in a week or more spreads to involve the entire gland in a diffuse, firm inflammatory process. That certainly sounds at this point like the picture in this case. The inflammatory process will classically depress thyroid function transiently to the extent that would be compatible with the decreased function indicated by a low uptake of the tracer dose of radioactive iodine in this case. The systemic manifestations may be a little more marked than they were in this woman, but on the other hand a number of cases of subacute thyroiditis have presented themselves with minimal systemic symptoms. This woman had a suggestion of some systemic effect from this inflammatory process, inasmuch as she had chills, although she had no known fever, in the week prior to entry. The fact that there was no tenderness, pain or subjective symptoms in the thyroid except slight pressure does tend to rule out this diagnosis, although again one could not be secure in accepting these as ruling out DeQuervain's disease. Although the majority of patients do have pain and tenderness, nevertheless some are completely asymptomatic as far as the local pathology is concerned.

I am left with a differential diagnosis between Hashimoto's struma and subacute thyroiditis of the DeQuervain type. It is rather difficult to choose, because there was one major finding against each of these two diseases; the rapid onset is against Hashimoto's disease and the absence of pain and tenderness is against DeQuervain's disease. Perhaps the one factor that would lead me to choose DeQuervain's disease rather than Hashimoto's struma is the rather marked suppression of thyroid function at this relatively early stage of the disease. Although myxedema may be a complicating factor in the end stages of Hashimoto's struma, this extreme degree of suppression of thyroid function would be unusual this early. In the cases of Hashimoto's struma that have been studied with radioactive iodine in this hospital, the lowest reported uptake was 15 per cent and the majority ran more or less in the normal range of I^{131} uptake.[2] Although neither of the diagnoses would be considered secure in this particular case, that one fact would tend to make me conclude with a diagnosis of subacute thyroiditis or pseudotuberculous, giant-cell or DeQuervain's thyroiditis, which are all the same disease.

I think I can see the headsman waiting with the ax.

Dr. Austin L. Vickery: Dr. Stanbury, you saw this patient.

Dr. John T. Stanbury: I think Dr. McDermott has gone more directly to the point than we did when the patient was here in the hospital. We have had very limited experience with acute and subacute thyroiditis in our clinic. We have seen a number of patients with Hashimoto's disease who have had a relatively normal accumulation of I^{131}, but the few patients we have seen who had thyroiditis, acute or subacute, commonly had a marked diminution in the I^{131} uptake. Our considerations were whether it was a rapidly growing small-cell carcinoma or a form of thyroiditis. Although we leaned toward the latter diagnosis, the patient was operated on with the former in mind.

Dr. Vickery: Dr. Arnold S. Jackson, who is a past president of the American Goiter Association, is a member of the group of surgeons from the Wisconsin Surgical Club visiting us today. Would you give us your opinion of the case, Dr. Jackson?

Dr. Arnold S. Jackson: I am impressed by the fact that we are seeing so many more cases of the thyroiditides now than we did twenty-five years ago. Two weeks ago I saw 3 cases. Also, since the thyroiditides blend from one type to another, there is disagreement among the pathologists about the type of each thyroiditis. The perithyroiditis that we see frequently is still another type. To me, the whole subject is growing more and more confusing, and I know less and less about it.

Clinical Diagnosis

Chronic thyroiditis.
?Small-cell carcinoma.

Dr. McDermott's Diagnosis

Subacute thyroiditis.

Anatomical Diagnosis

Subacute thyroiditis.

Pathological Discussion

Dr. Vickery: I saw this patient in the operating room when Dr. Oliver Cope was performing the procedure. He, unfortunately, is out of town and cannot give his own account of the operation. The outstanding finding was a hard lump in the right lobe, which was the initial symptom; this was sufficiently hard and firm that the question of malignancy was raised at that time. At the same time the left lobe was exposed; the same type of process was found to involve it as well as the isthmus. A frozen-section diagnosis of thyroiditis was made, confirming Dr. Cope's impression, and accordingly a subtotal thyroidectomy was performed. The first slide illustrates the gross specimen (Fig. 1), with the right and left lobes hemisected. You will see that there is practically no recognizable thyroid tissue in the whole gross section, most of it having been

Figure 1.

replaced by hard, whitish, fibrous-appearing tissue. In the left lobe, however, as you will recall from the protocol, the enlargement occurred after the right lobe had first been called to the patient's attention; here the process can be seen to be more central, with the periphery of the subtotally resected lobe quite intact, with normal-appearing thyroid, but this process is not sharply limited. One other thing to note in this slide is the fact that the capsule was intact about both of these lobes. Subacute thyroiditis, as Dr. McDermott has nicely described it, is unlike Riedel's struma, in that with the latter there is more sclerosis of the thyroid, with intimate adherence and involvement of the perithyroid structures.

Microscopically, this gland showed some residual thyroid tissue at the periphery that was not as yet involved in the subacute inflammatory process. Elsewhere, the typical microscopical picture was that of only a few scattered thyroid follicles remaining in what was otherwise a sea of rather dense connective tissue and chronic inflammatory infiltrate (Fig. 2). Here and there were focal areas of foreign-body-type giant-cell aggregations in the regions of degenerating acini. Here is a high-power view (Fig. 3) of what undoubtedly was the site of a previous follicle. Note the irregular area of pale-

Figure 2.

staining colloid surrounded by a circumferential ring of multinucleated giant cells. I think that from this picture you can appreciate why this process has been called by some a pseudotuberculous type of thyroiditis — because it does simulate tuberculosis. Also noted in the sections were foci of microabscesses, which are characteristically found in this entity. The etiology of subacute thyroiditis is obscure.

Dr. McDermott commented on the confusing terminology associated with this disease, and this has been elaborated on by Dr. Jackson. As a pathologist, I certainly can agree that the confusion exists. In a review of the subject by Crile and

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Rumsey[3] of the Cleveland Clinic 38 cases of subacute thyroiditis were discussed. The entity in their experience has not been as uncommon as in ours.

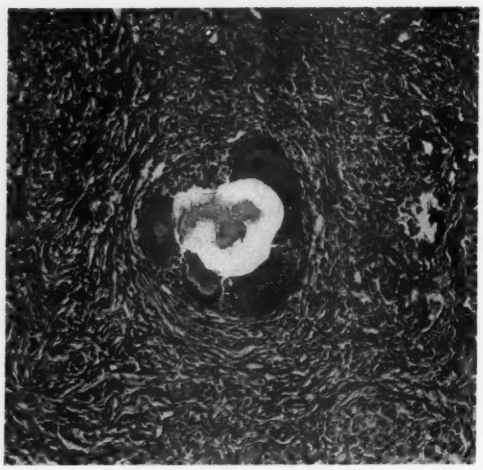

FIGURE 3.

Actually, in the last two and a half years, we have seen but three cases of subacute thyroiditis. The age incidence and the sex are of some interest. Most of these patients are around the middle age bracket, thirty to fifty years; the majority of them are female, just as in Hashimoto's disease. Chesky, Dreese and Hellwig[4] of the Hertzler Clinic recently reviewed some of their experience with chronic thyroiditis. They subdivided it in about the same manner that Crile and his co-workers do and as we do here, using chronic thyroiditis as a general term, with three main categories of classification: Hashimoto's struma, Riedel's struma and subacute thyroiditis. They reported 146 cases of Hashimoto's struma, 8 cases of Riedel's struma and 9 cases of subacute thyroiditis, identical to this case. Riedel's struma in our experience has been very uncommon.

The most important clinical feature of subacute thyroiditis is the diagnostic distinction from cancer, which often necessitates biopsy. Although subtotal thyroidectomy is the more common method of therapy, the Cleveland Clinic group prefer x-ray treatment.

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THE ANNUAL MEETING

THE one hundred and seventy-first annual meeting of the Massachusetts Medical Society will be held at the Hotel Statler, Boston, May 19–22. As usual, the afternoon and evening of the first day will be devoted entirely to business matters, the program of events of general interest beginning on the following morning. Thus the supervising censors will meet at 4:30 p.m. on May 19, their conference to be followed by the annual Cotting Supper for councilors at 6:00 p.m. and the annual meeting of the Council at 7:00 p.m. Concomitantly with the meeting of the censors, the Boston Medical Library will hold its annual meeting at 4:30.

In keeping with the hoary traditions of accumulated decades, the Committee on Arrangements, aided by the indefatigable executive secretary of the Society, has planned an ambitious program. Five general sessions will be held at which a variety of subjects will be presented by a carefully selected team of experts in their different fields; in addition, the sections of the Society on medicine, radiology, physical medicine, anesthesiology, obstetrics and gynecology, physiology and pathology, industrial health, surgery, dermatology, ophthalmology and otolaryngology and psychiatry and neurology will hold forth at luncheons on May 20, 21 and 22.

The official annual business meeting will take place on Tuesday, May 20, at 2:30 p.m. On this occasion the Secretary will report on the numerical changes in the membership of the Society and the President will give an account of his year's stewardship. Awards will be presented and any other business will be transacted that properly belongs within the province of the Society as a whole. The annual oration will conclude the meeting. On the following morning, at precisely 11:05 a.m., the Shattuck Lecture will be delivered by Dr. Derek E. Denny-Brown, James Jackson Putnam Professor of Neurology at Harvard Medical School and neurologist-in-chief at Boston City Hospital, on "The Changing Pattern of Neurological Medicine." At the Annual Dinner on May 21 the guest speaker will be Dr. John W. Cline, president of the American Medical Association.

According to custom, the usual scientific and technical exhibits will provide marvels on which to gaze as one perambulates; the Massachusetts Medico-Legal Society will hold its annual meeting on May 21; and an exhibition of works of art will be presented by the Massachusetts Physicians Art Association.

Meanwhile the annual meeting of the Woman's Auxiliary will take place at the Sheraton Plaza Hotel on May 20 and 21, opening with a business session on the morning of the first day, followed after lunch by a meeting of the Executive Committee. Mrs. Harold J. Wahlquist, president of the National Auxiliary, and the Honorable Philip J. Philbin of the Third Congressional District will be guest speakers at the luncheon. In the afternoon

tea will be served at the Society Headquarters, 22 Fenway.

On the second day of the meeting busses will carry the members to Marblehead, where luncheon will be served at the Adams House. After the luncheon a lecture will be given by Mrs. Laura S. Cochran, resident director of the John Robert Powers School, on "Six Secrets of the Powers Girls." It is expected that in the evening the ladies will be their husbands' guests at the annual dinner of the Society, and that the usual good time will be had by all.

EPIDEMIC HEMORRHAGIC FEVER

It is becoming commonplace for physicians and public-health workers to receive their first inkling of new developments in the fields of medicine, therapeutics and public health from either the lay press, the radio or the popular magazines. A few months ago, the occurrence of a new febrile illness that has been recognized among our troops in Korea was announced in this manner. It was revealed that late in the spring of 1951 an outbreak of a febrile illness, popularly referred to as Manchurian fever, occurred among our front-line combat troops. There were then said to be 187 proved cases, with 25 deaths, and perhaps a considerably greater number of ill-defined cases. A considerably larger number of cases have been recognized since then and the over-all case-fatality rate has recently been appreciably lower. Although the morbidity and mortality from this disease are relatively quite small when compared to those due to frostbite that occurred in the previous winter or to those due to infectious hepatitis, which has been plaguing the United Nations forces since the outbreak of the Korean conflict, there is considerable interest in this new condition because so little is known of its causative agents and of the means for coping with it.

The first seemingly authentic information concerning the disease became available in a mimeographed summary of the Japanese literature, dated August 13, 1951, prepared by Capt. Ralph M. Takami, Medical Intelligence and Epidemiology Officer, General Headquarters, Far East Command. A mimeographed report by Capt. John P. Craig, M.C., A.U.S., dated February, 1951, is also cited in the bibliography. This report has been summarized in the *Medical Newsletter of the United States Navy* of October 19, 1951. According to Takami's report, a number of Japanese medical officers described three outbreaks among their troops in Manchuria between 1939 and 1942. The outbreaks occurred in the autumn months; together they involved a total of 356 cases with 46 deaths, a mortality of 13 per cent. The disease was officially recognized as a new entity by the medical department of the Japanese army early in 1942; it was then called "epidemic hemorrhagic fever." Other outbreaks of the disease have probably occurred in these areas without being recognized, as some of its features resemble those of hemorrhagic purpura, atypical scarlet fever, typhus fever and acute nephritis.

The disease is known to occur in northern and northeastern Manchuria and probably also across the Soviet border in adjoining regions of Siberia. Until the present Korean outbreak, no other endemic areas were recognized, although the field rodent *Apodemus agrarius*, which is believed to be the chief reservoir of the causative agent, is found over the entire Korean peninsula. It was therefore considered that the infection was enzootic in Korea. The mite *Laelaps jettmari Vitzthum*, which is supposed to be the vector that transmits the agent from the field rodent to human beings, had not been found in Korea before the present war. One Japanese worker, however, is quoted as believing that the human body louse may also be a vector. Horses are also regarded as a possible reservoir of infection, but this has not been established, nor is it known how the disease might be transmitted from the horse to man.

The incidence of the disease reaches a peak in May and June and again in October and November, these being the months when the mites multiply most rapidly. Cases of the disease may occur at any time of the year, however, but they are known to recur in any given area during the same months of each year. The disease is particularly prevalent along river banks and in swamps and marshlands where grass grows high and unattended, providing an ideal habitat for field rats. Infection among troops is usually acquired in bivouacs or in the

lower floors of buildings, as are other mite-transmitted infections. It is also known to have occurred among troops exposed to hay that was brought in from certain endemic foci. The disease is probably not transmitted from person to person, no proved cases having been recorded among attendants, nurses, physicians or research workers.

The causative agent of epidemic hemorrhagic fever has been shown by Japanese workers to be a small filtrable virus that is not antigenically related to any other known virus. They demonstrated this agent in the blood of patients during the height of the fever but not after the fever had subsided. According to the Japanese investigators the virus remains viable in infected citrated blood stored at −3°C. for at least eight days; in emulsions of organs obtained from animals at the height of their fever the virus survives storage in dry ice (−70°C.) for eighty-one days. Monkeys are susceptible to subcutaneously injected virus in the form of ground-up infected mites or infected tissues; they develop a febrile illness, with characteristic pathological findings. Field rats, however, develop no clinical or anatomic changes when infected experimentally and are, therefore, thought to be capable of harboring inapparent infections from which the mite transmits the disease to man.

The bite of the mite that is responsible for human infection usually goes unnoticed and leaves no telltale eschar or regional lymphadenopathy. The incubation period varies from three days to a month, but it is usually two to three weeks. Prodromal symptoms may be present for one or two days, consisting of fatigue, anorexia, general malaise and slight myalgia. More often the onset is abrupt, with tremors, chills, fever, severe frontal headache, nausea and vomiting. The temperature rises to a peak of 104° or 105°F. by the third day and then falls, either by crisis or by rapid lysis, on the fifth or sixth day. Other manifestations may subsequently increase in severity; death, when it occurs, usually takes place one or two days after the temperature has fallen.

A morbilliform or petechial rash appears on the third day, involving the neck, axillas, upper arms and thorax; in severe cases it becomes more widespread. The face and neck may appear flushed, as with a fresh sunburn. Mucosal and subcutaneous hemorrhages occur, with severe injection of the corneal vessels. There may be slight edema of the face and some edema of the limbs. Headache, nausea, vomiting, hiccoughs, myalgia, arthralgia, insomnia and cerebral symptoms may be noted throughout the course. The cerebral manifestations may increase after defervescence and in severe cases may progress through delirium and coma. The pulse is relatively slow, but tachycardia may develop in serious cases. The blood pressure drops before or soon after the temperature declines. In the more severe cases there may be hemoptysis, hematemesis, hematuria and melena. Extensive renal damage may occur, resulting in anuria and uremia. The favorable cases gradually improve, the hemorrhages and albuminuria clearing first and the nausea, vomiting and hiccoughs subsiding later. In some cases, hemorrhagic manifestations may recur in cycles during convalescence.

Significant laboratory findings include albuminuria, hematuria, a decline in the phenolsulfonphthalein excretion and an increase in the blood nonprotein nitrogen. The red-cell count is high at first and then falls if there are diffuse hemorrhages, and there is a slight increase in the osmotic fragility of the erythrocytes. The white-cell count is low at first; it may later assume a leukemoid character, the total white-cell count rising as high as 80,000. Thrombocytopenia is also present, but eosinophils are usually seen throughout the course. The sedimentation rate does not increase, except slightly — late in the disease. There are no distinctive serologic findings.

Obviously, this is a disease that is potentially very serious. Much more information is needed concerning the causative agent, its reservoir and possible vectors and the manner in which it is transmitted to human beings. The prospects for combating or eliminating this disease depend on the early recognition of cases as they occur and on the success of epidemiologic and virologic studies, including the possibility of developing a protective vaccine. In the meantime, the preventive measures recommended involve the control of mites by the elimination of the rodent hosts from areas inhabited by troops. Residual miticides have also been sug-

gested for use in the field; some are available that might be applied to clothing.

It is the search for possible vectors and reservoirs of this infection that has given rise to the front-line story concerning United Nations soldiers' hunting rabbits and trapping and snaring rats and mice. Such activities have also been depicted by cartoonists who work among our troops or are acquainted with their activities. It is hoped that the hunting and trapping yielded enough material for the medical research workers to study during the winter months while the disease among the troops was not widely prevalent. Most of all it is hoped, of course, that the long-awaited armistice will materialize, so that during the next season, when such infections might be anticipated, it will no longer be necessary for troops to live under conditions that predispose to this infection. Meanwhile a group of distinguished investigators has proceeded to the area where the disease has been prevalent. They hope to acquire additional information and materials from fresh cases, should they occur during the present season. They will then be able to undertake intensive studies of the etiologic agent and epidemiology of the disease with a view to devising effective methods for its control.

HEALTH AND WEALTH IN OLD NEW YORK

A NEW arrangement between two major departments in the New York State Government is considered to be unique in the history of such establishments. This is the plan, recently put into execution, whereby the facilities of the Department of Social Welfare and those of the Department of Health will be co-ordinated in the supervision and inspection of the preventive and corrective health services provided annually for over 3,000,000 persons. These services are now rendered by more than 1500 agencies and institutions, voluntary and public, under the guidance of the State Department of Social Welfare.

The plan has been developed as a result of the studies made by the Interdepartmental Health Council, consisting of those state agencies responsible for health and medical services. The primary function of the Council is the co-ordination and integration of state facilities and resources to make them function more efficiently on their common problems. Over a third of the 3,000,000 patients concerned are public charges, receiving free care at a cost of $112,000,000 annually.

TOKEN OF AUTHORITY

NATURE tries to maintain a balance in all things. Winter gives way to summer. Floods are succeeded by the drying up of streams in their beds; every action, it is said, has its reaction. Even righteousness and evil fight on a battle line that ebbs and flows.

And now what may seem to many persons to be an almost classical example of this antiphonal relation has appeared. It is found in the announcement by the Secretary and General Manager of the American Medical Association that the trustees of that great body have been presented with a gavel made of wood from the recently reconstructed White House.

Is this significant, that they who have for so long knocked the Administration should now take the rap from the Executive Mansion itself?

Many substances impart to the urine a peculiar odor, and asparagus gives a very strong one. Numerous experiments lead to the belief that this excrementitial humor does not reach the bladder in its perfumed condition; that it only attains this when in contact with the atmosphere.

Boston M. & S. J., *May 5, 1852*

MASSACHUSETTS MEDICAL SOCIETY

ANNUAL MEETING OF THE COUNCIL

The annual meeting of the Council of the Massachusetts Medical Society will be held in the Georgian Room, Hotel Statler, on Monday, May 19, at 7:00 p.m.

Business:

1. Call to order at 7:00 p.m.
2. Presentation of record of meeting held February 6, 1952, as published in *The New England Journal of Medicine*, Supplement No. 1, Vol. 246, April 24, 1952.
3. Reports of standing and special committees.
4. Report of Committee on Nominations:

   President: Thomas H. Lanman, Suffolk
   President-Elect: Frederic Hagler, Hampden
   Vice-President: John J. Curley, Worcester North
   Secretary: H. Quimby Gallupe, Middlesex South
   Treasurer: Eliot Hubbard, Jr., Middlesex South
   Assistant Treasurer: Norman A. Welch, Norfolk
   Orator: Sara M. Jordan, Suffolk
5. Such other business as may legally come before the meeting.

H. Quimby Gallupe, M.D., *Secretary*

Councilors are asked to sign one of the two attendance books before the meeting. The Cotting Supper will be served immediately before the meeting.

DEATHS

Mongan — Charles E. Mongan, M.D., of Somerville, died on April 13. He was in his ninety-third year.

Dr. Mongan received his degree from Harvard Medical School in 1892. He was a former president of the Massachusetts Medical Society and a fellow of the American Medical Association.

He is survived by his widow and four children.

Winslow — Benjamin S. Winslow, M.D., of New Bedford, died on November 1, 1951. He was in his seventy-sixth year.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR MARCH, 1952

Résumé

Disease	March 1952	March 1951	Seven-Year Median
Chancroid	1	1	3
Chicken pox	1862	1781	2405
Diphtheria	3	10	20
Dog bite	692	847	847
Dysentery, bacillary	19	0	9
German measles	2146	154	224
Gonorrhea	131	145	274
Granuloma inguinale	0	0	0
Lymphogranuloma venereum	0	0	1
Malaria	4	0	7
Measles	11,909	1835	1835
Meningitis, meningococcal	9	5	7
Meningitis, Pfeiffer-bacillus	2	2	4
Meningitis, pneumococcal	3	4	3
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	1	0	0
Meningitis, undetermined	9	8	3
Mumps	1479	1758	1758
Poliomyelitis	2	1	1
Salmonellosis	10	5	8
Scarlet fever	520	560	703
Syphilis	203	117	226
Tuberculosis, pulmonary	217	214	225
Tuberculosis, other forms	17	20	20
Typhoid fever	1	2	1
Undulant fever	2	0	5
Whooping cough	217	195	592

Comment

Diseases below the seven-year median are chicken pox, diphtheria, mumps, scarlet fever and whooping cough.

The 3 diphtheria cases in March represent the lowest number ever reported for this month since 1906. Only once (in September, 1951) have fewer than 3 cases of diphtheria in one month been noted in our records.

Diseases markedly above the seven-year median are German measles and measles. The nineteen cases of bacillary dysentery reported in March represent delayed reports for January and February, 1952, covering three outbreaks; thus the high incidence in March is apparent rather than real.

As in February, 1952, German measles rose again in March to the highest level since 1943, but the total of 2146 cases was only about one fourth the number reported in March, 1943. This figure approaches the 2668 cases reported for the entire year of 1951 and the 2281 cases for the year 1950. It is the highest number of cases of German measles reported this season.

Measles has shown a very slight decrease since the record number of cases reported in February, 1952. The nearly 12,000 cases are still far above any number previously reported in March or in any month of any year in our records.

Geographical Distribution of Certain Diseases

The following diseases were reported from the communities named:

Diphtheria: Boston, 1; Watertown, 1; Weston, 1; total, 3.

Dysentery, bacillary: Grafton, 3; Westboro, 10; Wrentham, 6; total, 19.

Encephalitis, infectious: Hardwick, 1; Malden, 1; Princeton, 1; Quincy, 1; Seekonk, 1; Winthrop, 1; Worcester, 1; total, 7.

Hepatitis, infectious: Camp Edwards, 6; Fort Devens, 2; Haverhill, 1; Otis Air Force Base, 3; Somerville, 1; Wellesley, 2; Worcester, 21; Wrentham, 1; total, 37.

Lymphocytic choriomeningitis: Weymouth, 1; total, 1.

Malaria: Camp Edwards, 2; Fort Devens, 2; total, 4.

Meningitis, meningococcal: Cohasset, 1; Easthampton, 1; North Adams, 1; Quincy, 1; Stoneham, 1; Springfield, 3; Westford, 1; total, 9.

Meningitis, Pfeiffer-bacillus: Danvers, 1; Freetown, 1; total, 2.

Meningitis, pneumococcal: Brockton, 1; Framingham, 1; Melrose, 1; total, 3.

Meningitis, streptococcal: Malden, 1; total, 1.

Meningitis, undetermined: Chicopee, 1; Danvers, 1; Ipswich, 1; Northbridge, 1; Oxford, 1; Southbridge, 1; Wilmington, 1; Worcester, 2; total, 9.

Poliomyelitis: Camp Edwards, 1; Wayland, 1; total, 2.

Salmonellosis: Boston, 2; Cambridge, 1; Dedham, 2; Everett, 1; Haverhill, 1; Northampton, 1; Salem, 1; Watertown, 1; total, 10.

Septic sore throat: Belmont, 1; Boston, 2; Cambridge, 4; Dedham, 1; Melrose, 1; Quincy, 4; Warren, 2; Worcester, 2; total, 17.

Tetanus: Cambridge, 1; total, 1.

Trichinosis: Wellesley, 1; Worcester, 1; total, 2.

Typhoid fever: Springfield, 1; total, 1.

Undulant fever: Andover, 1; Belmont, 1; total, 2.

BOSTON MEDICAL LIBRARY ANNUAL MEETING

MONDAY AFTERNOON, MAY 19

Hotel Statler, Parlor C

4:30 p.m.

MASSACHUSETTS MEDICO-LEGAL SOCIETY ANNUAL MEETING

WEDNESDAY AFTERNOON, MAY 21

Hotel Statler, Parlor C

2:30 p.m.

EXHIBITION OF WORKS OF ART by Members of the Massachusetts Physicians Art Association

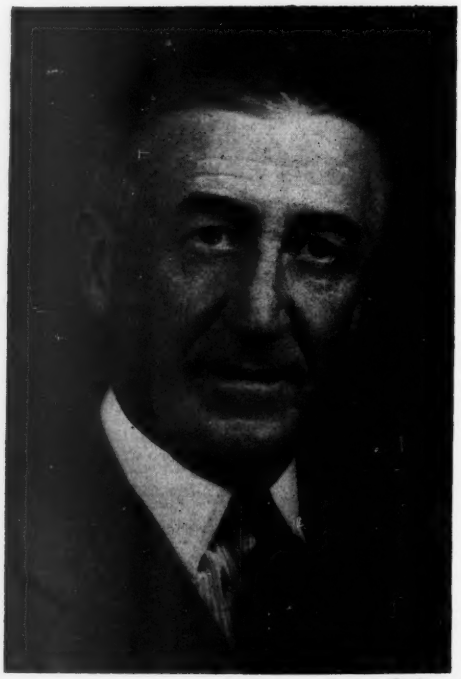
Hotel Statler, Fourth Floor

Daily: 9:00 a.m. — 5:00 p.m.

MAY 20, 21 and 22

STATE COLLEGE OF AGRICULTURE AND SCIENCE MANHATTAN KANSAS

OFFICERS OF THE MASSACHUSETTS MEDICAL SOCIETY, 1951–1952

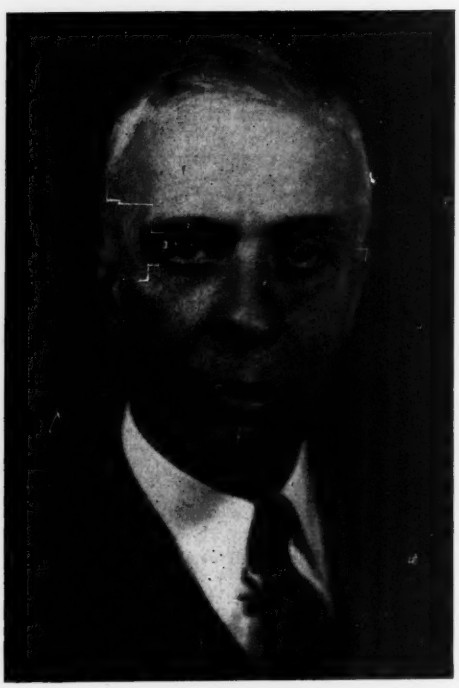


Bachrach

DR. THOMAS H. LANMAN, *President-Elect*

Bachrach

DR. W. RICHARD OHLER, *President*



DR. ALLEN G. RICE, *Vice-President*

PROGRAM OF THE ONE HUNDRED AND SEVENTY-FIRST ANNIVERSARY OF THE MASSACHUSETTS MEDICAL SOCIETY

Monday, Tuesday, Wednesday and Thursday, May 19, 20, 21 and 22

Hotel Statler, Boston

The Registration Desk will be located on the mezzanine floor, and all who attend the meeting are requested to register.

MONDAY AFTERNOON, MAY 19

4:30 **Supervising Censors' Meeting** (PARLOR B).

6:00 **Cotting Supper for Councilors** (PARLORS A AND B).

MONDAY EVENING, MAY 19

7:00 **Annual Meeting of the Council** (GEORGIAN ROOM).

TUESDAY MORNING, MAY 20

First General Session

GEORGIAN ROOM

9:00 *A Motion Picture Entitled "Gastrointestinal Cancer."*

9:25 *The Evaluation of Pilot Clinics.* DR. VLADO A. GETTING. Commissioner, Department of Public Health, Commonwealth of Massachusetts.

9:50 *The Problem of Obesity and Weight Control.* DR. JOSEPH ROSENTHAL. Assistant professor of medicine, Tufts College Medical School; staff member, New England Medical Center.

10:15 *The Use and Abuse of the Laboratory.* DR. PERRY J. CULVER. Associate in medicine, Harvard Medical School; assistant physician, Massachusetts General Hospital.

10:40 *The Use and Abuse of Heat Used Therapeutically.* DR. GEORGE MORRIS PIERSOL. Professor of physical medicine, School of Medicine, University of Pennsylvania; director, Department of Physical Medicine, University of Pennsylvania, Philadelphia, Pa.

11:05 *Roentgen Observation on Acute Abdominal Conditions.* DR. LEO G. RIGLER. Professor and chief, Department of Radiology, University of Minnesota, Minneapolis, Minn.

11:30 *Use and Abuse of Whole Blood Transfusions.* DR. JOHN ABAJIAN, JR. Professor of surgery (anesthesiology), University of Vermont College of Medicine; attending anesthetist, Mary Fletcher Hospital and Bishop DeGoesbriand Hospital, Burlington, Vt.

TUESDAY NOON, MAY 20

Section Meetings and Luncheons

12:00 m. — 2:00 p.m.

Section of Medicine

PARLOR A

The Relation of Internal Secretions to Growth. DR. JOSEPH AUB, *chairman*. Director, Huntington Laboratories, Massachusetts General Hospital; DR. IRA NATHANSON, Huntington Laboratories, Massachusetts General Hospital; DR. NATHAN B. TALBOT, physician, Children's Medical Service, Massachusetts General Hospital, and DR. GEORGE W. THORN, physician-in-chief, Peter Bent Brigham Hospital.

Section of Radiology

PARLOR B

Roentgen Studies of the Circulation of the Liver. DR. LEO B. RIGLER. Professor and chief, Department of Radiology, University of Minnesota, Minneapolis, Minn.

Section of Physical Medicine

PARLORS D AND E

Physical Medicine in Neuromuscular Conditions. DR. GEORGE MORRIS PIERSOL. Professor of physical medicine, School of Medicine, University of Pennsylvania; director, Department of Physical Medicine, University of Pennsylvania, Philadelphia, Pa.

Section of Anesthesiology

PARLOR C

Chronically Contracted Blood Volume and Adrenal Factors as Applied to Anesthesiology. DR. JOHN ABAJIAN, JR. Professor of surgery (anesthesiology), University of Vermont, College of Medicine; attending anesthetist, Mary Fletcher Hospital and Bishop DeGoesbriand Hospital, Burlington, Vt.

TUESDAY AFTERNOON, MAY 20

2:30 **Annual Meeting of the Massachusetts Medical Society** (GEORGIAN ROOM).

Presentation of Awards

Annual Oration (following annual meeting): *The New England Journal of Medicine* and the Massachusetts Medical Society. DR. JOSEPH GARLAND, Editor, *New England Journal of Medicine.*

WEDNESDAY MORNING, MAY 21

Second General Session

GEORGIAN ROOM

9:00 *A Motion Picture Entitled "Total Abdominal Hysterectomy and Perineorrhaphy."*

9:25 *Medicine + Industry = Occupational Health.* DR. J. F. MCCAHAN. Assistant secretary, Council on Industrial Health, American Medical Association.

9:50 *The Acute Abdomen in Pregnancy.* DR. ARTHUR J. WALLINGFORD. Professor of gynecology, Albany Medical College; head of Department of Obstetrics and Gynecology, Albany Hospital, Albany, N. Y.

10:15 *Infections of the Urinary Tract.* DR. MITCHELL I. RUBIN. Professor and head of the Department of Pediatrics, University of Buffalo School of Medicine; pediatrician-in-chief, Children's Hospital, Buffalo, N. Y.

10:40 *The Clinical Value of Needle Biopsy of the Liver.* DR. EDWARD A. GALL. Professor of pathology, College of Medicine, University of Cincinnati; director, Department of Pathology, Cincinnati General Hospital, Cincinnati, Ohio.

11:05 THE SHATTUCK LECTURE. The Changing Pattern of Neurological Medicine. DR. DEREK E. DENNY-BROWN. James Jackson Putnam Professor of Neurology, Harvard Medical School; neurologist-in-chief, Boston City Hospital.

WEDNESDAY NOON, MAY 21

Section Meetings and Luncheons

12:00 m. — 2:00 p.m.

Section of Obstetrics and Gynecology

PARLORS D AND E

Endometriosis. DR. ARTHUR J. WALLINGFORD. Professor of gynecology, Albany Medical College; head of Department of Obstetrics and Gynecology, Albany Hospital, Albany, N. Y.

Section of Pediatrics

PARLOR B

Kidney Functional Studies in Some Stress Situations in Children. DR. MITCHELL I. RUBIN. Professor and head of the Department of Pediatrics, University of Buffalo School of Medicine; pediatrician-in-chief, Children's Hospital, Buffalo, N. Y.

Section of Physiology and Pathology

PARLOR C

The Multicentric Origin of Cancer. DR. EDWARD A. GALL. Professor of pathology, College of Medicine, University of Cincinnati, Cincinnati, Ohio.

Section of Industrial Health

PARLOR A

Important Features in an Industrial Medical Program. DR. GEORGE F. WILKINS. Medical director, New England Telephone and Telegraph Company; president-elect, Industrial Medical Association.

WEDNESDAY AFTERNOON, MAY 21

Third General Session

GEORGIAN ROOM

Cardiac Symposium

2:00 *The Modern Management of Rheumatic Heart Disease.* DR. BENEDICT F. MASSELL. Associate research director, House of the Good Samaritan; chief, Rheumatic Fever Division, Children's Hospital.

2:25 *Surgery of the Mitral Valve.* DR. DWIGHT E. HARKEN. Assistant clinical professor of surgery, Harvard Medical School; surgeon, Peter Bent Brigham Hospital; surgeon and chief, Department of Thoracic Surgery, Mount Auburn Hospital.

2:50 *Control of Edema in Heart Disease.* DR. HERRMAN L. BLUMGART. Professor of medicine, Harvard Medical School; physician-in-chief, Beth Israel Hospital.

3:15 *Medical Aspects of Congenital Heart Disease.* DR. LEWIS DEXTER. Assistant professor of medicine, Harvard Medical School; senior associate in medicine, Peter Bent Brigham Hospital.

3:40 *Surgical Treatment of Congenital Heart Disease.* DR. J. GORDON SCANNELL. Instructor in surgery, Harvard Medical School; assistant surgeon, Massachusetts General Hospital.

4:05 *Treatment of Acute Myocardial Infarction.* DR. LAURENCE B. ELLIS. Assistant clinical professor of medicine, Harvard Medical School; chief, Cardiac Clinic, Boston City Hospital.

4:30 *A Motion Picture Entitled "Coarctation of the Aorta."*

Courtesy of E. R. Squibb & Sons.

WEDNESDAY EVENING, MAY 21

6:00–7:00 **Cocktail Party** (BAY STATE ROOM).

7:00 **Annual Dinner of the Massachusetts Medical Society** (GEORGIAN ROOM).

Presiding: DR. W. RICHARD OHLER, president, Massachusetts Medical Society.

Guest Speaker:

DR. JOHN W. CLINE, president, American Medical Association.

Ladies may be invited to attend the dinner.

Tickets for the cocktail party and dinner *must* be procured in advance.

THURSDAY MORNING, MAY 22

Fourth General Session

GEORGIAN ROOM

9:00 *A Motion Picture Entitled "We Speak Again — The Rehabilitation of the Laryngectomized."*

9:25 *Ear, Nose and Throat Cancer Comes to the General Practitioner.* DR. DANIEL MILLER. Instructor in otolaryngology, Tufts College Medical School; assistant surgeon, Massachusetts Eye and Ear Infirmary.

9:50 *The Diagnosis of Primary Malignant Tumors of Bone.* DR. G. EDMUND HAGGART. Orthopedic surgeon, New England Baptist and New England Deaconess hospitals; chief of orthopedic surgery, Lahey Clinic.

10:15 *Accidental Electrocution.* DR. RICHARD FORD, assistant professor of legal medicine, Harvard Medical School; medical examiner, Southern District, Suffolk County.

10:40 *How Good Is the Surgical Repair of the Common Hernia? — An Appraisal of 800 Operations After 2-5 Years.* DR. JONATHAN E. RHOADS. Professor of surgery and surgical research, School of Medicine, University of Pennsylvania; chief, Surgical Division II, Hospital of the University of Pennsylvania, Philadelphia, Pa.

11:05 *Obstacles to the Cure of Psychosomatic Conditions.* DR. O. SPURGEON ENGLISH. Professor and head of the Department of Psychiatry, Temple University Medical School and Hospital, Philadelphia, Pa.

11:30 *Principles Guiding the Treatment of Acute Dermatitis.* DR. CHESTER N. FRAZIER. Edward Wigglesworth Professor of Dermatology, Harvard Medical School; chief, Dermatological Service, Massachusetts General Hospital.

THURSDAY NOON, MAY 22

Section Meetings and Luncheons

12:00 m — 2:00 p.m.

Section of Surgery

PARLOR B

Plasma Expanders. DR. JONATHAN E. RHOADS. Professor of surgery and surgical research, School of Medicine, University of Pennsylvania; chief, Surgical Division II, Hospital of the University of Pennsylvania, Philadelphia, Pa.

Section of Dermatology

PARLORS D AND E

Trivia of Disease: Some Thoughts on External Remedies. DR. CHESTER N. FRAZIER. Edward Wigglesworth Professor of Dermatology, Harvard Medical School; chief, Dermatological Service, Massachusetts General Hospital.

Section of Ophthalmology and Otolaryngology

PARLOR C

Orbital Lesions, Diagnosis, Prognosis and Treatment. DR. VIRGIL G. CASTEN. Associate in ophthalmology, Harvard Medical School; ophthalmic surgeon, Massachusetts Eye and Ear Infirmary and Massachusetts General Hospital.

Section of Psychiatry and Neurology

PARLOR A

Introducing the Psychiatric Treatment in Psychosomatic Illness. DR. O. SPURGEON ENGLISH. Professor and head of the Department of Psychiatry, Temple University School of Medicine and Hospital, Philadelphia, Pa.

THURSDAY AFTERNOON, MAY 22

Fifth General Session

GEORGIAN ROOM

Symposium: Present Status of Recent Therapeutic Advances

2:00 *Drug Therapy of Anemia.* DR. WILLIAM B. CASTLE. Director, Thorndike Memorial Laboratory; director, Second and Fourth Medical Services, Boston City Hospital.

2:25 *Newer Problems in the Treatment of Infections.* DR. LOUIS WEINSTEIN. Associate professor of medicine, Boston University School of Medicine; lecturer in infectious diseases, Harvard Medical School; chief, Infectious Disease Service, Massachusetts Memorial Hospitals.

2:50 *The Practical Management of Rh Problems.* DR. FRED H. ALLEN, JR. Instructor in pediatrics, Harvard Medical School; associate director, Blood Grouping Laboratory of Boston; associate hematologist, Children's Hospital and Boston Lying-in Hospital.

3:15 *Sex Hormone Therapy in Gynecology.* DR. JOHN ROCK. Clinical professor of gynecology, Harvard Medical School; senior surgeon, Free Hospital for Women, Brookline.

3:40 *Clinical Uses for ACTH and Cortisone.* DR. GEORGE W. THORN. Hersey Professor of the Theory and Practice of Physic, Harvard Medical School; physician-in-chief, Peter Bent Brigham Hospital.

4:05 *Selection of Anti-Infective Agents in the Prevention and Treatment of Disease.* DR. CHESTER S. KEEFER. Wade Professor of Medicine, Boston University School of Medicine; physician-in-chief, Massachusetts Memorial Hospitals; director, Evans Memorial Hospital.

4:30 *A Motion Picture Entitled "Injuries to the Peripheral Nerves."*

SCIENTIFIC EXHIBITS

BOOTH NO.

9 — LIBRARY ACTIVITIES.
Sponsor: The Boston Medical Library.

65 — HIP-JOINT CHANGES IN SPINA BIFIDA.
Sponsor: Massachusetts Hospital School, Canton, Mass.
Exhibitors: Dr. H. E. Pratt, Dr. John J. Foley and Dr. Roger J. C. Robert.

66–67 — SURGERY OF THE PANCREAS.
Sponsor: The Lahey Clinic.
Exhibitors: Dr. Richard B. Cattell and Dr. Kenneth W. Warren.

82 — RADIOISOTOPES IN CANCER RESEARCH.
Sponsor: Cancer Research Institute of the New England Deaconess Hospital.
Exhibitor: Dr. Shields Warren.

83 — PRESENT STATUS OF THE TREATMENT OF HYPERTENSIVE DISEASE.
Sponsor: Massachusetts Memorial Hospitals and Boston University School of Medicine.
Exhibitors: Dr. Reginald H. Smithwick, Dr. Robert M. Wilkins, Dr. George Levene, Dr. George P. Whitelaw, Dr. Dera Kinsey, Dr. William E. R. Greer and Dr. Jesse E. Thompson.

84 — EYE BANK. MASSACHUSETTS EYE AND EAR INFIRMARY.
Sponsor: Section on Ophthalmology and Otolaryngology.
Exhibitors: Dr. Edwin B. Dunphy and Dr. Garrett Sullivan.

85 — REPAIR OF HYPOSPADIAS.
Sponsor: Children's Medical Center.
Exhibitor: Dr. Donald W. MacCollum.

86 — SLIPPED CAPITAL FEMORAL EPIPHYSES.
Sponsor: Orthopedic Department, Massachusetts General Hospital.
Exhibitors: Dr. Armin Klein, Dr. Robert J. Joplin, Dr. John A. Reidy and Dr. Joseph Hanelin.

87 — A COLOR ARCADE OF THE COMMON DERMATOSES.
Exhibitor: Dr. George E. Morris.

88 — THE EFFECT OF RADIATION UPON THE GROWTH AND DEVELOPMENT OF THE SPINE.
Sponsor: Department of Radiology, Children's Medical Center.
Exhibitors: Dr. Martin H. Wittenborg, Dr. Jonathan Cohen and Dr. Edward B. D. Neuhauser.

89 — THE CONTROL OF DIABETES.
Sponsor: The Joslin Clinic.
Exhibitors: Dr. Elliott P. Joslin, Dr. Howard F. Root, Dr. Priscilla White, Dr. Alexander Marble, Dr. Allen P. Joslin and Dr. Robert F. Bradley.

90 — PHYSICAL MEDICINE FOR THE NEUROLOGIC PATIENT — ELECTRODIAGNOSIS, TREATMENT OF FLACCID AND SPASTIC PARALYSIS.
Sponsor: Massachusetts General Hospital.
Exhibitor: Dr. Arthur L. Watkins.

91 — OSTEOID OSTEOMA IN CHILDREN — THE CAUSE OF BIZARRE PAIN IN CHILDREN.
Sponsor: Children's Medical Center.
Exhibitors: Dr. William T. Green and Dr. Jonathan Cohen.

CORRIDOR — SPLENECTOMY IN THE BLOOD DYSCRASIAS.
Sponsor: The New England Center Hospital and Pratt Diagnostic Clinic.
Exhibitors: Dr. C. Stuart Welch and Dr. William Dameshek.

CORRIDOR — SOCIETY ACTIVITIES.
Sponsor: The Massachusetts Medical Society.

PARLOR — RADICAL RESECTION FOR CARCINOMA OF THE STOMACH. (Three-dimensional moving picture.)
Sponsor: The Lahey Clinic.
Exhibitor: Dr. Samuel Marshall.
Courtesy of Ethicon Suture Laboratories.

TECHNICAL EXHIBITORS

	BOOTH NO.
Abbott Laboratories	33 & 34
Alkalol Company	25
Ames Company, Inc.	45
Doris Appel Medical Sculptures	13
Ayerst, McKenna & Harrison, Ltd.	29

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Brewer & Company, Inc. ..... 4 & 5
Brown and Connolly, Inc. 65
Buffington's, Inc. 40
Camel Cigarettes ..... 13 & 14
Cardiotron (Samuel Mushlin) 8-A
Carnation Company 59
Ciba Pharmaceutical Products, Inc. 41
Coca-Cola Company ..... 16 & 17
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Davies, Rose & Company, Ltd. 22
Denver Chemical Manufacturing Company, Inc. 74
Desitin Chemical Company 50
Dietene Company 71
Doho Chemical Corporation, Inc. 2
S. F. Durst & Company, Inc. 72
Dy-Dee Service, Inc. 12
Eaton Laboratories, Inc. 24
Endo Products, Inc. 55
C. B. Fleet Company, Inc. 48
General Electric X-Ray Corporation 5
Gerber's Baby Foods 78
Lawrence E. Gott 23
J. E. Hanger, Inc. 6
Hanovia Chemical & Manufacturing Company 7-A
Dan Hibel, Inc. ..... Stage C & D
Hoffmann-La Roche, Inc. 43
Ives-Cameron, Inc. 35
George Laben ..... 31 & 32
Lederle Laboratories Division 69
Eli Lilly and Company 20
E. F. Mahady Company ..... Stage A & B
M & R Dietetic Laboratories, Inc. 60
McNeil Laboratories, Inc. 80
Medical Clearing Bureau, Inc. 61
Medical Protective Company 30
The Wm. S. Merrell Company 39
The National Drug Company 38
New England Dairy & Food Council, Inc. 28
T. J. Noonan Company 15
Otis Clapp & Son, Inc. 3
Parke, Davis & Company 7
E. L. Patch Company 19
Pet Milk Company 79
Charles Pfizer & Company, Inc. 64-A
Philip Morris & Company, Ltd., Inc. 52
Pitman-Moore Company 77
Professional Supply Company 8
L. & B. Reiner 1
A. H. Robins, Inc. 46
Rystan Co., Inc. 53
Sanborn Company 58
Sandoz Pharmaceuticals 57
Saratoga Springs Authority 10
Schering Corporation 56
G. D. Searle & Company 70
Sharp & Dohme, Inc. 62
Smith, Kline & French Laboratories 63
E. R. Squibb & Sons 47
Surgeons and Physicians Supply Company 76
Tailby-Nason Company 21
Travenol Laboratories, Inc. 64
U. S. Vitamin Corporation 26
Varick Pharmacal Company 51
Walker Laboratories, Inc. 92
Warner-Hudnut, Inc. 68
White Laboratories, Inc. 36
Winthrop-Stearns, Inc. 54
Wyeth, Inc. 42

NOTICES

THE NEW ENGLAND CARDIOVASCULAR SOCIETY

The Henry Jackson Lecture of the New England Cardiovascular Society will be given by Dr. Helen B. Taussig, physician-in-charge of the Cardiac Clinic at Johns Hopkins Hospital. Dr. Taussig's subject will be "The Management of the Cyanotic Child and Indications for Operation." The lecture, which will be preceded by a brief business meeting, will be presented on May 12, at 8:15 p.m., in the Boston Medical Library Auditorium, 8 Fenway, Boston. Interested physicians, medical students and members of the New England Postgraduate Assembly are invited to attend.

NEW ENGLAND DIABETES ASSOCIATION

The New England Diabetes Association will hold its annual meeting on May 15, at 8 p.m., in the main auditorium of Peter Bent Brigham Hospital, Boston. Dr. Edward S. Dillon, associate professor of metabolic diseases, University of Pennsylvania Graduate School of Medicine, will speak on "Tuberculosis and Diabetes." Discussers will be Dr. Theodore L. Badger, associate in medicine at Harvard Medical School, and Dr. Norman J. Wilson, instructor in surgery at Tufts College Medical School.

SOCIETY MEETINGS AND CONFERENCES

MAY 1–3. American College Health Association. Page 634, issue of April 17.

MAY 3. New England Society of Anesthesiologists. Page 595, issue of April 10.

MAY 3. Boston University School of Medicine Alumni Association. Page 560, issue of April 3.

MAY 3–31. Springfield Hospital. Page 635, issue of April 17.

MAY 4–9. Society for Pediatric Research and the American Pediatric Society. Hotel Chamberlain, Old Point Comfort, Virginia.

MAY 7. Massachusetts Society of Examining Physicians. Page 595, issue of April 10.

MAY 8. The Choice of Patients for the Surgical Treatment of Hypertension. Dr. James A. Evans. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

MAY 8–10. American Neurological Association. Page 559, issue of April 3.

MAY 9–JUNE 3. Boston City Hospital House Officers' Association. Page 634, issue of April 17.

MAY 10. Boston Dispensary Proctologic Session. Page 433, issue of March 13.

MAY 10 AND 11. American Electroencephalographic Society. Page 390, issue of March 6.

MAY 11–17. Pan-American Convention of Gastroenterology. Page 434, issue of March 13.

MAY 12. New England Cardiovascular Society. Notice above.

MAY 13. Springfield Academy of Medicine. Page 635, issue of April 17.

MAY 13. New England Society of Anesthesiologists. Page 635, issue of April 17.

MAY 13 AND 20. Children's Cancer Research Foundation. Page 676, issue of April 24.

MAY 15. New England Diabetes Association. Notice above.

MAY 15–17. American College of Surgeons. Page 596, issue of April 10.

MAY 19–22. Massachusetts Medical Society. Page 716.

DISTRICT MEDICAL SOCIETIES

HAMPSHIRE

MAY 7. Annual Meeting. Jones Library, Amherst.

NORFOLK

MAY 7. Harvard Club. 6:00 p.m.

(*Notices concluded on page xv*)